



NEPHRO-PROTECTIVE EFFECT OF METHANOL EXTRACT OF BAUHINIA TOMENTOSA IN GENTAMICIN INDUCED NEPHROTOXICITY IN WISTAR RATS

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Abstract:

Bauhinia TomENTOSA known for its various medicinal properties is also a natural antioxidant and a freeradical scavenger with no documented evidence as a nephro protective agent. To evaluate the nephroprotective activity of methanol extract of *Bauhinia TomENTOSA* seeds in a rodent model of gentamicin induced nephrotoxicity. Gentamicin treatment caused nephrotoxicity as evidenced by marked elevation in serum urea, serum uric acid, serum creatinine and blood urea nitrogen (107.5 ± 16.92 mg/dl, 0.8 ± 0.09 mg/dl, 3.05 ± 0.29 mg/dl, 47.8 ± 9.07 mg/dl) respectively when compared to the saline treated groups. Co-administration of *Bauhinia TomENTOSA* extract with gentamicin decreased the rise in these parameters in a dose dependent manner. Histopathological analysis revealed epithelial loss with intense granular degeneration in gentamicin treated rats, whereas aqueous extract of *Bauhinia TomENTOSA* mitigated theseverity of gentamicin-induced renal damage.

Key words: *Bauhinia tomentosa*, Nephroprotective activity, methanolextarct, Gentamycin induced nephrotoxicity.

Introduction:

Recognition of drug-induced nephrotoxicity as a significant contributor to kidney disease including acute kidney injury (AKI) and chronic kidney disease (CKD) has gained increasing momentum in recent times. Nephrotoxicity constitute a whole gamut of disorders reflecting damage to different nephron segments as a consequence of individual drug mechanisms. Consequences of drug toxicity might include both glomerular and tubular injuries leading to acute or chronic functional changes. [1-3]. The frequency of drug-induced nephrotoxicity is approximately 14-26% in adult populations as detailed in previous prospective cohort studies. Aminoglycosides [4-6], a commonly used group of antibiotics top the causality chart in drug induced nephrotoxicity. However, nephrotoxicity induced by them continue to be a challenge as it results in kidney damage by a direct dose dependent mechanism. Gentamicin induced acute renal failure has proved to be an excellent working animal model for exploring the pathogenesis of drug induced acute renal failure and has resulted in animpetusto develop therapeutic approaches to minimize or prevent its harmful effects in humans. Stem bark of *Bauhinia* upgrade the impact of Anti-tubercular medications utilized as a part of instance of Tubercular Cervical Lymphadenitis. *B. tomentosa*. Demonstrates the counter ulcer movement against gastric ulcer prompted. The root bark is vermifuge, It is used internally to treat conditions of the large intestine, An infusion of the root bark is used as an external application to treat inflamed glands, abscesses and skin conditions The stem bark is astringent [7-9]. It is used as a gargle for the mouth, the flowers are used as a remedy for dysentery and diarrhea, The fruit is said to be diuretic, The seed is eaten as a tonic and aphrodisiac and The seed is eaten as a tonic and aphrodisiac etc.



PHYTOCHEMICAL SCREENING, ANTIOXIDANT AND HEPATO PROTECTIVE ACTIVITY OF METHANOL EXTRACT OF BAUHINIA TOMENTOSA

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ABSTRACT:

The main objective of the study is to evaluate hepatoprotective activity of Methanolic extract of Bauhinia tomentosa against paracetamol induced hepatotoxicity using Albino Wistar rats weighing 150-200 g. Silymarin (100 mg/kg) orally was used as standard drug. Test groups received methanolic extract of Bauhinia tomentosa in the doses of 200, 300 and 400 mg/kg/day orally along with paracetamol for 7 days. The hepatoprotective effect of methanolic extract of Bauhinia tomentosa was evaluated by assessment of biochemical parameters viz; Serum glutamate pyruvate transaminase (SGPT), serum glutamate oxaloacetate transaminase (SGOT), alkaline phosphatase (ALP), low density lipoproteins (LDL), high density lipoproteins (HDL), bilirubin, cholesterol and triglycerides were measured. Histopathological examination of the liver was also done. Methanolic extract of Bauhinia tomentosa (300 mg/kg and 300 mg/kg) exhibited highly significant result in biochemical evaluation. Histopathological examination of the liver suggested hepatoprotective effect of the extract by decreasing the extent of centrilobular necrosis, fatty changes and congestion of sinusoids when compared to paracetamol group. Methanolic extract of Bauhinia tomentosa showed significant dose dependent protection against paracetamol induced liver injury in rats

Key words: Bauhinia tomentosa, hepatoprotective activity, biochemical parameters, SGPT, SGOT, ALP, HDL

Introduction:

Medicinal plants have been utilized in the treatment of various pathological diseases and neurological disorders for many years in folk medicine[1]. The therapeutic plants, in addition, were found to be safe and free from side effects when compared with modern medicines. Several scientific studies demonstrated that the principle bioactive compounds present in the medicinal plants were the main causative agents for their predominant therapeutic effects. Even though 80% of drugs used in developing countries such as India and China are derivatives of phytoextracts, the rational treatment of neurological disorders by plant extract derived drugs is still in its embryonic stage due to the complex chemistry and organization of the central nervous system. Extracts were found to be better than purified compounds since they contain many phytoconstituents which may work synergistically to protect against many disease. Bauhinia tomentosa is a yellow orchid tree, belonging to the family Caesalpinaceae. It is an erect, branched shrub with 6-12 m height and pale lemon yellow flowers. It is commonly known as 'Kanchini' in Tamil and 'Phalgu'[2] in Sanskrit. The generic name denotes the bauhin brothers, Jean and Gaspard, the Swiss botanist; and the species name 'tomentosa' denotes its hairy and velvety pods. It flowers in rainy season and fruits in winter season. It has been used traditionally for its therapeutic



A STUDY ON ANTI-HEPATOTOXIC EFFECT OF BAHUINIA TOMENTOSA LINN AGAINST PARACETAMOL

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ABSTRACT

The need for an antidote from the herbal industry is a common factor because chemical-induced hepatotoxicity is a major threat to human life in today's modern world. Even drugs that are easy to get hold of and readily available can cause side effects when used irrationally. Bauhinia tomentosa Linn is a member of the fabaceae family and is thought to be one such potential agent that contains a wide range of chemical compounds with both therapeutic and antidote properties. In this study, Bauhinia tomentosa Linn was extracted using ethyl alcohol, and the resulting ethanolic extract was tested for its ability to protect albino mice's livers from Acetaminophen-induced liver damage. The biochemical assessment, histo obsessive examinations are filled in as record for the evaluation of hepatoprotective movement.

KEYWORDS: Bauhinia tomentosa, Hepatoprotective, Paracetamol toxicity.

INTRODUCTION

Hepatotoxicity is a major pharmacological defect caused by the drugs has been an important reason for the withdrawal and banning of many drugs in the market. Liver unique organ play a major role in the metabolism and biotransformation of xenobiotics and food substances that enter the body¹. A significant amount of deaths occur due to diseases aggravated by the toxic action of therapeutic substances prescribed by allopathic system on the liver. This situation warrants us to find out remedies for hepatotoxicity. Herbal remedies are safe and effective in restoration process with no or less side effects. The vast diversity of plant kingdom encourages for herbal research and the medicinal properties of many plants are yet to be explored. Efficacy testing of the traditional / new herbal products by experimental screening method is an important tool to establish standard therapeutic profile. However, there should be adequate data from in vivo and in vitro studies to validate the claimed therapeutic potential of testing substance. A reliable model to find out hepatoprotective efficacy of herbal preparations is paracetamol induced hepatotoxicity evaluation in albino mice as per earlier literatures.

LITERATURE REVIEW

Sanjay V. Satpute (2020) Traditional herbal medicine is a chief source of biologically active compounds needed for the treatment of human ailments. There are many more medicinal plant species used as folklore medicine, but very few attempts has been made so far to validate those c medicinal plants is necessary for wider acceptance all over the world. Authentication and scientific validation of medicinal plant is a fundamental requirement of industry and other organizations dealing with herbal drugs.

Sandeep B. Subramanya et al (2018) Acetaminophen (APAP), which is also known as paracetamol or N-acetyl-p-aminophenol is a safe and potent drug for fever, pain and inflammation when used at its

**PHARMACOECONOMICS OF INSULIN ANALOGUES PRESCRIBED IN DIABETES MELLITUS PATIENTS IN A TERTIARY CARE HOSPITAL****Satish Gunda^{1*}, Dr.V.Jayashree²**

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Abstract— About 90% of all instances of diabetes worldwide are of type 2, which is the most prevalent form of the disease. Diabetes treatment is costly and on the rise all around the world. The WHO predicts that over the next 20 years, the cost of managing diabetes would nearly double, rising from 234 billion in 2007 to 411 billion. An analysis to ascertain the economic impact of the recommended treatment option in tertiary care hospital in northern India given the incidence and consequences of diabetes. In this study, oral hypoglycemic medications that are used to treat diabetes mellitus will be subjected to a pharmacoeconomic analysis. Patients with type 2 diabetes mellitus (T2DM) need anti-diabetic medications on an ongoing basis, frequent blood glucose monitoring, and a variety of laboratory tests, all of which place a huge financial burden on the diabetes patients and the global economies. This study's objectives were to determine the economic impact of various anti-diabetic therapies recommended to patients with T2DM in a tertiary care hospital in north India and analyse the prescribing patterns to highlight the current approaches to the rational use of anti-diabetic drugs in T2DM patients visiting the medicine out-patient department.

Keywords— *Pharmacoeconomics Insulin, Analogues Prescribed, Diabetes, Mellitus, Patients, Tertiary Care Hospital.*

INTRODUCTION

The incidence of both type 1 and type 2 diabetes is increasing worldwide, with type 2 diabetes prevalence increasing quicker due to increased obesity, sedentary lifestyle, and an increasing share of the ageing population as a result of better medical facilities. kind 2 diabetes is the most common kind of diabetes, accounting for over 90% of all diabetes occurrences worldwide. Diabetes treatment is costly and rising globally. According to WHO, the global cost of managing diabetes is anticipated to nearly double from 234 billion in 2007 to 411 billion in the next two decades. Diabetes and its accompanying cardiovascular and cerebrovascular problems are expected to cost the country an estimated 336.6 USD in lost national GDP over the next decade. According to a 2016 WHO study, 63% of all fatalities in India were caused by noncommunicable diseases (NCDs), with diabetes accounting for 3% and other noncommunicable diseases accounting for 13%. Noncommunicable diseases accounted for more disability-adjusted life years (DALYs) in India in 2010 than communicable illnesses - roughly 235 million against 222 million DALYs, respectively. From 30.5% in 1990 to 55.4%

Initiation and Evaluation of Drug Information Services at a Tertiary Care Teaching Hospital in South Telangana

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Adepu *et al.*: Evaluation of Drug Information Services in South Telangana

Drug information service is the provision of written or verbal information about safe use of medications or drug therapy in response to a request from any health care professional. A prospective observational pilot study was initiated at a 1000 bed tertiary care teaching hospital to create an awareness, implementation and evaluation of the drug information services. Institutional ethics committee has approved the study and the hospital authorities permitted the service. The drug information service activity was started at clinical pharmacy department in the hospital and Pharm. D interns and the faculty was involved in the study. Drug information queries were collected during ward rounds and also through direct access. The ultimate question was analyzed after receiving the query, suitable references were reviewed and the final answer was synthesized and the approved answer was provided to the requester. Periodically the quality assurance of the information provided was assessed using quality assurance check list. A total of 154 queries were received during the study period. Most of the queries (69) belong to the category of drug of choice. Majority queries came from general medicine (45 %) and emergency medicine departments (16 %). Post graduate students (40 %) and medical interns (38 %) were the major requesters. Both verbal and written answers were provided to 136 queries. Majority queries received were during ward rounds and answers were provided within 8 h. The quality assurance score for the randomly selected queries was found 4.9 out of 5 indicate good quality service. The study findings suggest that drug information services were well utilized by the health care professionals. However, there is a need to create awareness among all health care professionals regarding usefulness of this service.

Key words: Drug information service, health care professional, query, response, quality assurance

Society of Hospital Pharmacists of Australia (SHPA), defines drug information as "the provision of written and/or verbal information or advice about drugs and drug therapy in response to a request from other health care providers, organizations, committees, patients or members of the public"^[1]. The whole objective of this service is to provide accurate, unbiased, factual information, primarily in response to patient-oriented problems. Lack of unbiased information is one of the major causes of irrational use of drugs leading to therapeutic failure and adverse drug reactions. It is very difficult for any healthcare provider to be updated with increasing therapeutic information explosion both in print and electronic media to choose appropriate medications for treatment and to provide right information to the patients about the medications prescribed. In the era of "evidence-based medicine" practice, the role of

Drug Information Center (DIC) is becoming highly important and the services are appreciated^[2].

Drug Information Service (DIS) is well advanced in developed countries like the United States, Australia and United Kingdom (UK). The first official DIC was started in 1962 at University of Kentucky Medical center with sole purpose of offering comprehensive information on drugs to staff physicians and dentists to evaluate and compare the information on drugs to be provided to the nursing staff^[3].

But in developing countries, it is still a new concept. In India, provision of drug information is

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Development, characterization, and enhancement of bioavailability with improved Enzalutamide (BCS Class II) formulations by employing novel principles of nanotechnology and their cytotoxic evaluation

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ABSTRACT:

Prostate cancer is the most commonly diagnosed non-cutaneous malignancy in men in western and most developing countries. Enzalutamide (EZT) is an antineoplastic hormonal agent primarily used in the treatment of locally advanced and metastatic prostate cancers. In the present study, the aim was to develop a nanoparticle, and liposomal-based delivery system to target prostate cancer cells. This involved the development of aEZT loaded with Chitosan, Cyclodextrin and PLGA based Nanoparticles and EZT loaded with HCD, DCP based Liposomes formulations in an attempt to improve the therapeutic efficacy of EZT in prostate cancer and to mitigate its toxicity. The particles with a uniform size distribution and spherical shape were developed. Liposomal formulations showed a pronounced cytotoxic effect on PC3, LNCaP, VCaP, cellscancer cells. The superior cell-killing effect of the Liposomal formulations may be attributable to their sustained drug-release characteristics and high cellular internalization. The results were also found to significantly increase in the bioavailability achieved by the F16 and F20 liposomal formulations inhibit colony formation in cell lines. Furthermore, the androgen based castrateresistant prostate cancer can be treated with EZT liposomal formulations with enhanced bioavailability, by indicating the cell apoptosis-inducing potential of EZT liposomes. Overall, these results suggest that liposomal-based formulations of EZT exhibit superior anticancer activity and have enormous potential in the treatment of prostate cancers.

Key words: Enzalutamide, Prostate cancer, liposomes, Nanoparticles.

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Design and Fabrication of Oral Fast Dissolving Film of Tramadol Hydrochloride

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ABSTRACT: -

For the preceding two decades, there has been a heightened demand for more patient-compliant dosage forms. Modern progresses in the technology have offered viable dosage substitutions from oral route for pediatrics, geriatric, bedridden, nauseous or noncompliant patients. Buccal drug delivery has newly become a chief mode of drug administration. Due to fast dissolution it affords sooner onset of action, sidestepping the first pass metabolism, dropping gastric degradation and metabolism of drugs and thus enhance their oral bioavailability. These properties of oral films with patient convenience and compliance made prevalent and accepted dosage form for pediatric and geriatric as well as adult residents.

Keywords: -Mouth dissolving film, Hydrophilic polymers, Formulation consideration, Manufacturing techniques, Evaluation parameters.

INTRODUCTION: -

The definitive aim of every drug conveyance system is the efficacious delivery of the drug, in which practically 90% of the drugs are directed to the body for the action of numerous sicknesses and disease as it is observed as the harmless, most suitable and most inexpensive method of drug delivery having the uppermost patient compliance. Fast dissolving oral films or oral wafers or oral strips or sublingual strips or oral thin films are the greatest forward-thinking form of oral solid dosage form due to more elasticity and coziness. [1] It progresses the usefulness of active pharmaceutical requirements by liquefying it within a minute of oral cavity after the interaction with saliva deprived of chewing and no necessity of water for administration. It provides speedy absorption and prompt bioavailability of drugs due to extraordinary blood flow and permeability of oral mucosa is 4-1000 times superior than that of skin. [2,3] Fast dissolving oral films are advantageous in patients such as pediatric, geriatrics, incapacitated, emetic patients, diarrhea, sudden period of allergic attacks or coughing for those who have an energetic life style. [4,5] The practice of such dosage form is likewise valuable whether indigenous accomplishment desired such as local anesthetic for toothaches, oral ulcers, cold sores or teething. At present, Tramadol is accessible in the form of tablet, infusion as well as capsules in the market. Some pediatric and geriatrics patients are non-cooperative with these dosage forms. [6] From now oral disintegrating films have become important tool to improve the patient compliance.

Tramadol hydrochloride is a centrally acting synthetic opioid analgesic binding to specific opioid receptors. It is castoff in the supervision of long-lasting pain and is suggested as chief line drug in the treatment of postoperative or orthopedic damage induced acute pain. The contemporary effort is planned to formulate and estimate oral fast dissolving film of tramadol hydrochloride as an innovative arrangement of continued analgesia for patients with orthopedic wounds. The drug possessions of tramadol hydrochloride are entirely appropriate on the drug selection criteria of the mouth dissolving film. Tramadol hydrochloride is fits to BCS class-I as it is having extraordinary solubility and high permeability which is tolerable for preparation of mouth dissolving film.

ANATOMY OF ORAL CAVITY: -

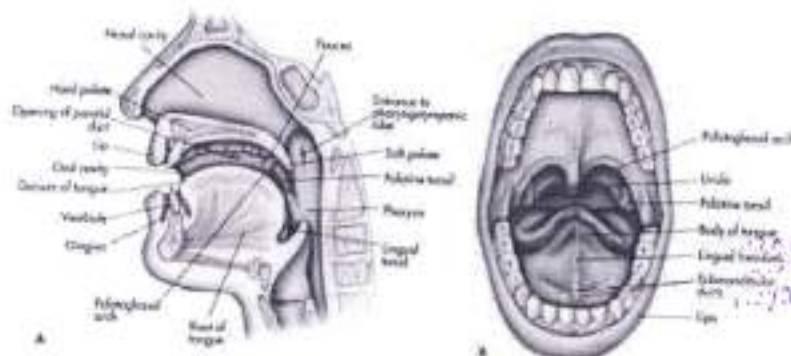



Fig 1-> Anatomy of oral cavity


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ANTIDIABETIC ACTIVITY OF POLYHERBAL FORMULATION IN DEXAMETHASONE INDUCED DIABETES IN WISTAR ALBINO RATS

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ABSTRACT

Background: Diabetes mellitus (DM) is a group of disorders that results in too much sugar in the blood due to impairment of lipids, carbohydrates, proteins metabolism.

Aim and objectives: Development and Evaluation of Polyherbal formulation (PHF) and determination of antidiabetic potential of developed formulation in Dexamethasone induced animal model.

Method: In the present study plant parts *Azadirachta indica* (AI) leaves, *Moringa Oleifera* (MO) fruits and *Andrographis paniculata* (AP) root and stem were collected and evaluated as per physico-chemical parameters and active chemical constituents were extracted using hydroalcoholic solvent. The active compounds present in all the three extracts were identified by preliminary phytochemical screening. PHF was prepared in a ratio of 1:1:1 quality of the finished product was evaluated on the parameter's angle of repose, loose bulk density, tapped bulk density, carr's index and hausner ratio as per the World Health Organisation's (WHO) guidelines for the quality control of herbal materials. The acute toxicity study of PHF were performed as per OECD guideline 423, rats were orally administered 250, 500, 1000 and 2000mg/kg over 14 days. The oral glucose tolerance test (OGTT) was performed at 200 and 400mg/kg body weight. Antidiabetic activity of the PHF (200 and 400mg/kg) was screened against Dexamethasone (DXM) induced diabetes in rats and glibenclamide was used (5.0mg/kg body weight) as standard drug. The investigational drug was administered for 14 days and the effect of the PHF on blood glucose levels was studied at 14th day after interventional period. At the end of the study, the blood samples were collected from all the animals for biochemical estimation.

Result: The plant parts AI leaves, MO fruits, AP stem and leaves were evaluated as per physicochemical parameters and they were found as per API. Preliminary phytochemical screening of hydroalcoholic extracts were revealed that presence of alkaloids, glycosides, saponins, flavonoids, carbohydrates, steroids, tannins and phenolic compounds in each extract. PHF were developed by mixing of each extract in the same ratio and evaluated. It was found to be angle of repose (θ) 29.1, loose bulk density 0.48gm/ml, tapped density 0.54gm/ml, carrs index 12.50%, hausner's ratio 1.13. Diabetes was induced by DXM and treated with PHF did not show any change in behavior and no mortality was observed during interventional period upto the dose level 2000mg/kg. OGTT was performed by oral administration of PHF with dose 200 and 400mg/ kg body weight result was found to be gradually decreased in blood glucose level 75.75 ± 1.92 mg/dl and 72 ± 2.73 mg/dl at 180min from the study it was predicted that PHF possess Anti-hyperglycemic activity. Experimental study was shows that on repeated administration of PHF and glibenclamide for 14 days, a sustained and significant decrease in the average blood glucose level of diabetic rats was observed. End of the interventional period biochemical parameters were studied, and it was found to be level of SGOT and urea level remain constant at dose of 200mg/kg, decrease in SGPT is near to standard and decrease in creatinine level is greater than Std at dose of 400mg/kg.

Conclusion: PHF containing extracts of (*Azadirachta indica*, *Moringa oleifera* and *Andrographis paniculata*) showed significant antidiabetic and antihyperlipidemic activity which was close to standard drug. Along with remarkable reduction in Total Cholesterol (TC) level and increased in High Density Lipoprotein (HDL) DXM induced diabetes rats. The formulation has emerged as potential combination which can challenge the synthetic drug.

Keywords: Diabetes mellitus; *Azadirachta indica*; *Moringa oleifera*; *Andrographis paniculata*; Polyherbal formulation, Glibenclamide

INTRODUCTION

Importance of Herbal in Mankind

Herbal drugs play an important role in the development of potent therapeutic agents. Furthermore, it has proven their potential for the prevention of several ailments. Earlier human beings started their studies on diseases and its treatments, but there was no evidence found that people have prehistoric use of synthetic medicines for their sickness [1]. However, they



Synthesis, Analgesic and Anti-Inflammatory Activities of Some Pyrazolo[3,4-c]Pyrazole Derivatives

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Abstract—Historically, heterocyclic compounds containing Nitrogen, and their derivatives have been invaluable as a source of therapeutic agents. Pyrazole, with two nitrogen atoms and aromatic character, provides diverse functionality and stereochemical complexity in a five-membered ring structure. In Knorr pyrazole synthesis, diimine compound gets deprotonated to regenerate the acid catalyst and provide the final pyrazole product. Formation of pyrazole derivatives from hydrazines, hydrazides, semicarbazides, thiosemicarbazide and aminoguanidines by condensation with 1,3-dicarbonyl compounds is possible. As fused pyrazoles are reported to be well known pharmacophores, this has motivated to synthesize some of the pyrazolopyrazole derivatives by using hydrazine hydrate, thiosemicarbazide and semicarbazide. A series of 3-(aryl)-4-methyl-3a,6-dihydropyrazolo[3,4-c]pyrazole-2(3H)-carboxamides (IVa3-e3), 3-(aryl)-4-methyl-3a,6-dihydropyrazolo[3,4-c]pyrazole-2(3H)-carbothioamide (IVa2-e2) and 4-(aryl)-3-methyl-1,3a,4,5-tetrahydropyrazolo[3,4-c]pyrazoles (IVa1-e1) were synthesized by conventional method where fused pyrazolopyrazoles were prepared. All the compounds were synthesized with good yield (56-81 %) and characterized by IR, ¹H NMR spectral data and C, H, N elemental analysis. All the synthesized compounds exhibited analgesic and anti-inflammatory activities.

Keywords—analgesic, anti-inflammatory, knorr pyrazole synthesis, pyrazole, pyrazolo[3,4-c]pyrazole.

Introduction

Pyrazole refers to the significant [1] class of simple aromatic ring organic compounds of the heterocyclic series characterized by a 5-membered ring structure composed of three carbon atoms and two nitrogen atoms in adjacent positions [2- 4]. Being so composed and having pharmacological effects on humans, they are classified as alkaloids, although they are rare in nature. In 1959, the first natural pyrazole, 1-pyrazolyl- alanine, was isolated from seeds of watermelons. Nitrated-pyrazole-based energetic compounds have attracted wide publicity in the field of energetic materials [5]. The term

pyrazole was given by Ludwig Knorr in 1883. Researchers synthesized pyrazole scaffold and studied their applications in Alzheimer's Disease and Parkinson's Disease Treatment [6]. Formation of pyrazole derivatives from hydrazines, hydrazides, semicarbazides and aminoguanidines by condensation with 1,3-dicarbonyl compounds is possible. Pyrazole derivatives have a long history of application in agrochemicals and pharmaceutical industry as herbicides and active pharmaceuticals. Thienopyrazole Moieties are also proved effective [7]. Pyrazoles have been the recent target of numerous methodologies, mostly due to their prevalence as scaffolds in drug discovery programs as antimicrobials [8- 9] as HMG-CoA reductase inhibitors, as inhibitors of HIV-1 reverse transcriptase and synthesis in particular of bioactive compounds and reactions in different media. The pyrazole ring is present as the core in a variety of leading drugs such a Celebrex, Viagra or Rimonabant. Pyrazoles are found to possess anti-inflammatory [10- 11] and analgesic [10, 12] activities. Many attempts were made by researchers to find out able potent pyrazolo-pyrazole derivatives [13-16] and applications [17] of pyrazoles and related compounds to enhance the biological activity.

Materials and Methods

Well dried apparatus was used to conduct the reactions requiring anhydrous conditions. Laboratory reagent grade solvents and reagents used and purified by distillation and crystallization wherever necessary. Open capillary method was used for determining melting points of newly synthesized compounds. The final products were purified by recrystallization and purity was checked by micro TLC.

The IR spectra of the compounds were recorded on JASCO FT/IR-5300 spectrometer using KBr pressed pellet. ¹H NMR spectra were recorded in a BRUKER DPX-200MHz spectrometer using TMS as internal standard. Perkin Elmer 2400 elemental analyzer was used for analysis of C, H and N which were found within ± 0.4 % of the theoretical values.

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Simultaneous Estimation of Netipitant and Palonosetron using UPLC

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Abstract:- A simple and selective LC method is described for the determination of Netipitant and Palonosetron in tablet dosage forms. Chromatographic separation was achieved on a Inertsil ODS (C18) RP Column (250mm x 4.6 mm, 5 μ m) column using mobile phase consisting of a 55 volumes of mixed phosphate buffer and 45 volumes of acetonitrile were prepared with detection of 253nm. Linearity was observed in the range 25-125 μ g/ml for Netipitant ($r^2 = 0.995$) and 50-150 μ g/ml for Palonosetron ($r^2 = 0.999$) for the amount of drugs estimated by the proposed methods was in good agreement with the label claim. The proposed methods were validated. The accuracy of the methods was assessed by recovery studies at three different levels. Recovery experiments indicated the absence of interference from commonly encountered pharmaceutical additives. The method was found to be precise as indicated by the repeatability analysis, showing %RSD less than 2. All statistical data proves validity of the methods and can be used for routine analysis of pharmaceutical dosage form.

Keywords: palonosetron, netipitant, acetonitrile, inertsil ODS, repeatability..

INTRODUCTION

Netipitant competitively binds to and blocks the activity of the human substance P/NK1 receptors in the central nervous system (CNS), thereby inhibiting NK1-receptor binding of the endogenous tachykinin neuropeptide substance P (SP), which may result in the prevention of chemotherapy-induced nausea and vomiting (CINV). It is N,N,2-Dimethyl-N-[4-(2-methylphenyl)-6-(4-methylpiperazin-1-yl)pyridin-3-yl]propanamide. Its molecular weight is 578.603 mg/mol. (M, manoranjani.2019)

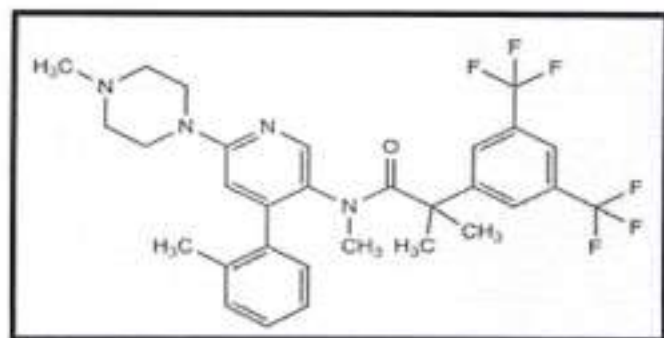


Fig 1. Structure of Netipitant

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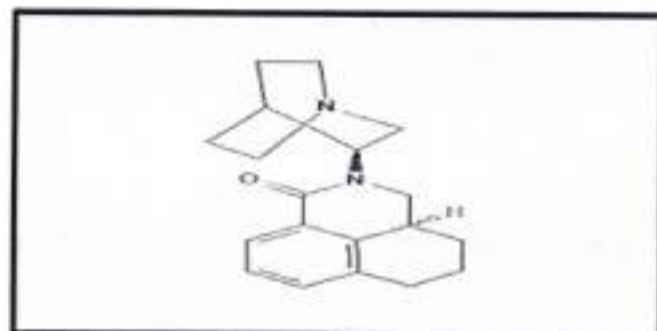


Fig 2. Structure of Palonosetron



Synthesis, Analgesic and Anti-Inflammatory Activities of Some Pyrazolo[3,4-c]Pyrazole Derivatives

¹S.Jayanthimala, ²G.Mahesh, ³Nimmala Shanthi, ⁴P.Nagamani

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Abstract—Historically, heterocyclic compounds containing Nitrogen, and their derivatives have been invaluable as a source of therapeutic agents. Pyrazole, with two nitrogen atoms and aromatic character, provides diverse functionality and stereochemical complexity in a five- membered ring structure. In Knorr pyrazole synthesis, diimine compound gets deprotonated to regenerate the acid catalyst and provide the final pyrazole product. Formation of pyrazole derivatives from hydrazines, hydrazides, semicarbazides, thiosemicarbazide and aminoguanidines by condensation with 1,3-dicarbonyl compounds is possible. As fused pyrazoles are reported to be well known pharmacophores, this has motivated to synthesize some of the pyrazolopyrazole derivatives by using hydrazine hydrate, thiosemicarbazide and semicarbazide. A series of 3-(aryl)-4-methyl- 3a,6-dihydropyrazolo[3,4-c]pyrazole-2(3H)-carboxamides (IVa3-e3), 3- (aryl)-4-methyl-3a,6-dihydropyrazolo[3,4-c]pyrazole-2(3H)-carbothioamide (IVa2-e2) and 4-(aryl)-3-methyl-1,3a,4,5- tetrahydropyrazolo[3,4-c]pyrazoles (IVa1-e1) were synthesized by conventional method where fused pyrazolopyrazoles were prepared. All the compounds were synthesized with good yield (56-81 %) and characterized by IR, ¹H NMR spectral data and C, H, N elemental analysis. All the synthesized compounds exhibited analgesic and anti- inflammatory activities.

Keywords—analgesic, anti-inflammatory, knorr pyrazole synthesis, pyrazole, pyrazolo[3,4-c]pyrazole.

Introduction

Pyrazole refers to the significant [1] class of simple aromatic ring organic compounds of the heterocyclic series characterized by a 5-membered ring structure composed of three carbon atoms and two nitrogen atoms in adjacent positions [2- 4]. Being so composed and having pharmacological effects on humans, they are classified as alkaloids, although they are rare in nature. In 1959, the first natural pyrazole, 1-pyrazolyl- alanine, was isolated from seeds of watermelons. Nitrated-pyrazole-based energetic compounds have attracted wide publicity in the field of energetic materials [5]. The term

pyrazole was given by Ludwig Knorr in 1883. Researchers synthesized pyrazole scaffold and studied their applications in Alzheimer's Disease and Parkinson's Disease Treatment [6]. Formation of pyrazole derivatives from hydrazines, hydrazides, semicarbazides and aminoguanidines by condensation with 1,3-dicarbonyl compounds is possible. Pyrazole derivatives have a long history of application in agrochemicals and pharmaceutical industry as herbicides and active pharmaceuticals. Thienopyrazole Moieties are also proved effective [7]. Pyrazoles have been the recent target of numerous methodologies, mostly due to their prevalence as scaffolds in drug discovery programs as antimicrobials [8- 9] as HMG-CoA reductase inhibitors, as inhibitors of HIV-1 reverse transcriptase and synthesis in particular of bioactive compounds and reactions in different media. The pyrazole ring is present as the core in a variety of leading drugs such a Celebrex, Viagra or Rimonabant. Pyrazoles are found to possess anti-inflammatory [10- 11] and analgesic [10, 12] activities. Many attempts were made by researchers to find out able potent pyrazolo-pyrazole derivatives [13- 16] and applications [17] of pyrazoles and related compounds to enhance the biological activity.

Materials and Methods

Well dried apparatus was used to conduct the reactions requiring anhydrous conditions. Laboratory reagent grade solvents and reagents used and purified by distillation and crystallization wherever necessary. Open capillary method was used for determining melting points of newly synthesized compounds. The final products were purified by recrystallization and purity was checked by micro TLC.

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Simultaneous Estimation of Netipitant and Palonosetron using UPLC

P. Nagamani¹, S. Jayanthimala², G. Mahesh³, Nimmala Shanthi⁴

Department of Pharmaceutical Sciences, Vikas College of Pharmaceutical Sciences,
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Keywords: palonosetron, netipitant, acetonitrile, inertsil ODS, repeatability..

INTRODUCTION

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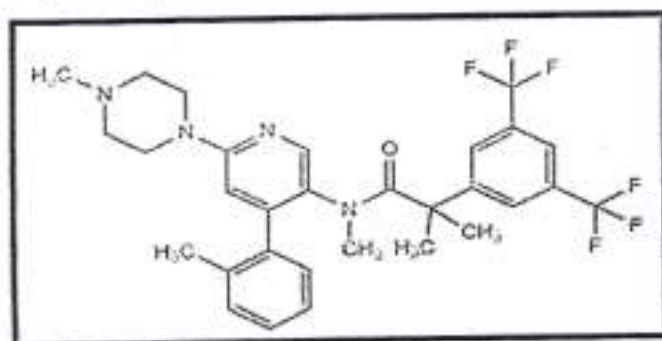


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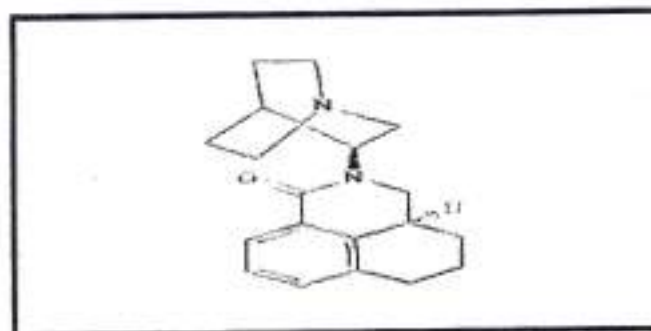


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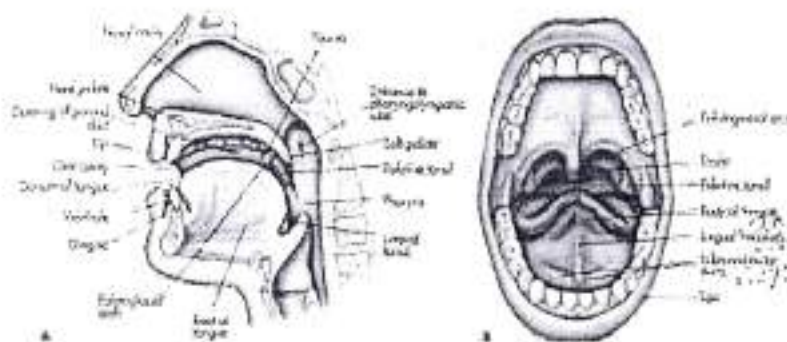


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ANTIDIABETIC ACTIVITY OF POLYHERBAL FORMULATION IN DEXAMETHASONE INDUCED DIABETES IN WISTAR ALBINO RATS

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Background: Diabetes mellitus (DM) is a group of disorders that results in too much sugar in the blood due to impairment of lipids, carbohydrates, proteins metabolism.

Aim and objectives: Development and Evaluation of Polyherbal formulation (PHF) and determination of antidiabetic potential of developed formulation in Dexamethasone induced animal model.

Method: In the present study plant parts *Azadirachta indica* (AI) leaves, *Moringa Oleifera* (MO) fruits and *Andrographis paniculata* (AP) root and stem were collected and evaluated as per physico-chemical parameters and active chemical constituents were extracted using hydroalcoholic solvent. The active compounds present in all the three extracts were identified by preliminary phytochemical screening. PHF was prepared in a ratio of 1:1:1 quality of the finished product was evaluated on the parameter's angle of repose, loose bulk density, tapped bulk density, carr's index and hausner ratio as per the World Health Organization's (WHO) guidelines for the quality control of herbal materials. The acute toxicity study of PHF were performed as per OECD guideline 423, rats were orally administered 250, 500, 1000 and 2000mg/kg over 14 days. The oral glucose tolerance test (OGTT) was performed at 200 and 400mg/kg body weight. Antidiabetic activity of the PHF (200 and 400mg/kg) was screened against Dexamethasone (DXM) induced diabetes in rats and glibenclamide was used (5.0mg/kg body weight) as standard drug. The investigational drug was administered for 14 days and the effect of the PHF on blood glucose levels was studied at 14th day after interventional period. At the end of the study, the blood samples were collected from all the animals for biochemical estimation.

Result: The plant parts AI leaves, MO fruits, AP stem and leaves were evaluated as per physicochemical parameters and they were found as per API. Preliminary phytochemical screening of hydroalcoholic extracts were revealed that presence of alkaloids, glycosides, saponins, flavonoids, carbohydrates, steroids, tannins and phenolic compounds in each extract. PHF were developed by mixing of each extract in the same ratio and evaluated. It was found to be angle of repose (θ) 29.1, loose bulk density 0.48gm/ml, tapped density 0.54gm/ml, carr's index 12.50%, hausner's ratio 1.13. Diabetes was induced by DXM and treated with PHF did not show any change in behavior and no mortality was observed during interventional period upto the dose level 2000mg/kg. OGTT was performed by oral administration of PHF with dose 200 and 400mg/kg body weight result was found to be gradually decreased in blood glucose level 75.75 ± 1.92 mg/dl and 72 ± 2.73 mg/dl at 180min from the study it was predicted that PHF possess Anti-hyperglycemic activity. Experimental study was shows that on repeated administration of PHF and glibenclamide for 14 days, a sustained and significant decrease in the average blood glucose level of diabetic rats was observed. End of the interventional period biochemical parameters were studied, and it was found to be level of SGOT and urea level remain constant at dose of 200mg/kg, decrease in SGPT is near to standard and decrease in creatinine level is greater than Std at dose of 400mg/kg.

Conclusion: PHF containing extracts of (*Azadirachta indica*, *Moringa oleifera* and *Andrographis paniculata*) showed significant antidiabetic and antihyperlipidemic activity which was close to standard drug. Along with remarkable reduction in Total Cholesterol (TC) level and increased in High Density Lipoprotein (HDL) DXM induced diabetes rats. The formulation has emerged as potential combination which can challenge the synthetic drug.

Keywords: Diabetes mellitus; *Azadirachta indica*; *Moringa oleifera*; *Andrographis paniculata*; Polyherbal formulation, Glibenclamide

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Herbal drugs play an important role in the development of potent therapeutic agents. Furthermore, it has proven their potential for the prevention of several ailments. Earlier human beings started their studies on diseases and its treatments, but there was no evidence found that people have prehistoric use of synthetic medicines for their sickness [1]. However, they

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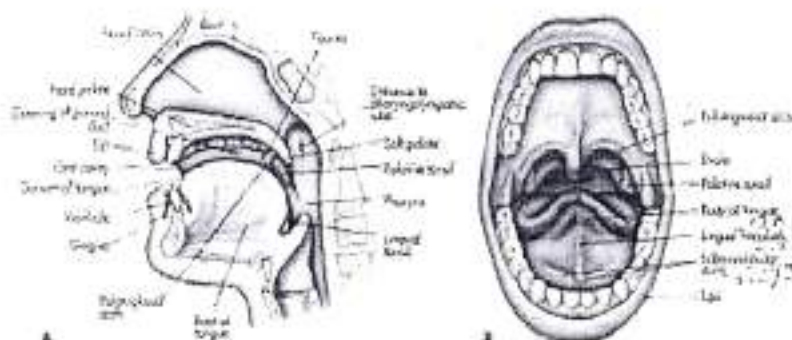


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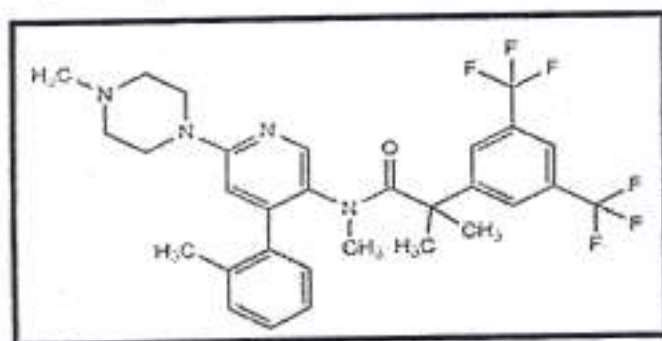


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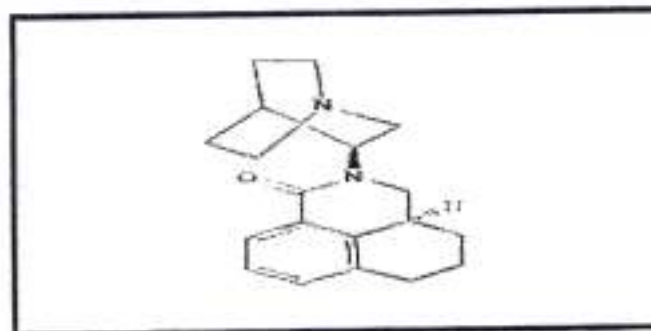


Fig 2. Structure of Palonosetron

Simultaneous Estimation of Netipitant and Palonosetron using UPLC

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Abstract:- A simple and selective LC method is described for the determination of Netipitant and Palonosetron in tablet dosage forms. Chromatographic separation was achieved on a Inertsil ODS (C18) RP Column (250mm x 4.6 mm, 5 μ m) column using mobile phase consisting of a 55 volumes of mixed phosphate buffer and 45 volumes of acetonitrile were prepared with detection of 253nm. Linearity was observed in the range 25-125 μ g/ml for Netipitant ($r^2 = 0.995$) and 50-150 μ g/ml for Palonosetron ($r^2 = 0.999$) for the amount of drugs estimated by the proposed methods was in good agreement with the label claim. The proposed methods were validated. The accuracy of the methods was assessed by recovery studies at three different levels. Recovery experiments indicated the absence of interference from commonly encountered pharmaceutical additives. The method was found to be precise as indicated by the repeatability analysis, showing %RSD less than 2. All statistical data proves validity of the methods and can be used for routine analysis of pharmaceutical dosage form.

Keywords: palonosetron, netipitant, acetonitrile, inertsil ODS, repeatability..

INTRODUCTION

Netipitant competitively binds to and blocks the activity of the human substance P/NK1 receptors in the central nervous system (CNS), thereby inhibiting NK1-receptor binding of the endogenous tachykinin neuropeptide substance P (SP), which may result in the prevention of chemotherapy-induced nausea and vomiting (CINV). It is N,N,2-Dimethyl-N-[4-(2-methylphenyl)-6-(4-methylpiperazin-1-yl)pyridin-3-yl]propanamide. Its molecular weight is 578.603 mg/mol. (M, manoranjani.2019)

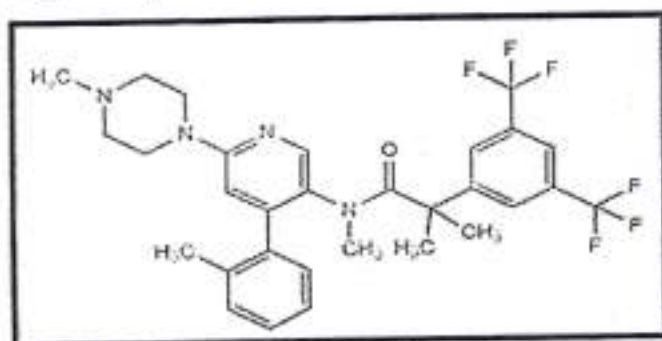


Fig 1. Structure of Netipitant

Palonosetron is a 5-HT₃ receptor antagonist with a strong binding affinity for this receptor and little or no affinity for other receptors. Cancer chemotherapy may be associated with a high incidence of nausea and vomiting, particularly when certain agents, such as cisplatin, are used. It is (5S)-3-[(3S)-1-azabicyclo[2.2.2]octan-5-yl]-3-azatriacyclo[7.3.1.0]trideca-1(12),9(13),10-trien-2-one. Its molecular weight is 296.407 g/mol (Suman et al 2020).

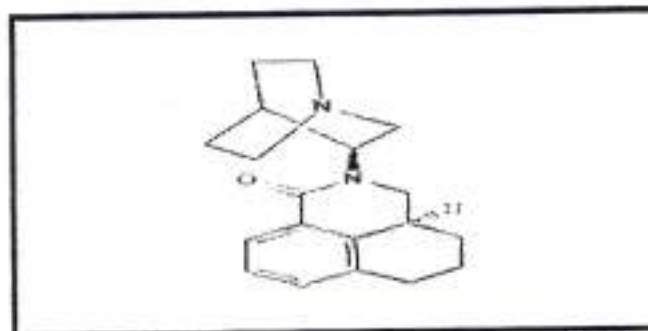


Fig 2. Structure of Palonosetron

ANTIDIABETIC ACTIVITY OF POLYHERBAL FORMULATION IN DEXAMETHASONE INDUCED DIABETES IN WISTAR ALBINO RATS

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ABSTRACT

Background: Diabetes mellitus (DM) is a group of disorders that results in too much sugar in the blood due to impairment of lipids, carbohydrates, proteins metabolism.

Aim and objectives: Development and Evaluation of Polyherbal formulation (PHF) and determination of antidiabetic potential of developed formulation in Dexamethasone induced animal model.

Method: In the present study plant parts *Azadirachta indica* (AI) leaves, *Moringa Oleifera* (MO) fruits and *Andrographis paniculata* (AP) root and stem were collected and evaluated as per physico-chemical parameters and active chemical constituents were extracted using hydroalcoholic solvent. The active compounds present in all the three extracts were identified by preliminary phytochemical screening. PHF was prepared in a ratio of 1:1:1 quality of the finished product was evaluated on the parameter's angle of repose, loose bulk density, tapped bulk density, carr's index and hausner ratio as per the World Health Organization's (WHO) guidelines for the quality control of herbal materials. The acute toxicity study of PHF were performed as per OECD guideline 423, rats were orally administered 250, 500, 1000 and 2000mg/kg over 14 days. The oral glucose tolerance test (OGTT) was performed at 200 and 400mg/kg body weight. Antidiabetic activity of the PHF (200 and 400mg/kg) was screened against Dexamethasone (DXM) induced diabetes in rats and glibenclamide was used (5.0mg/kg body weight) as standard drug. The investigational drug was administered for 14 days and the effect of the PHF on blood glucose levels was studied at 14th day after interventional period. At the end of the study, the blood samples were collected from all the animals for biochemical estimation.

Result: The plant parts AI leaves, MO fruits, AP stem and leaves were evaluated as per physicochemical parameters and they were found as per API. Preliminary phytochemical screening of hydroalcoholic extracts were revealed that presence of alkaloids, glycosides, saponins, flavonoids, carbohydrates, steroids, tannins and phenolic compounds in each extract. PHF were developed by mixing of each extract in the same ratio and evaluated. It was found to be angle of repose (θ) 29.1, loose bulk density 0.48gm/ml, tapped density 0.54gm/ml, carrs index 12.50%, hausner's ratio 1.13. Diabetes was induced by DXM and treated with PHF did not show any change in behavior and no mortality was observed during interventional period upto the dose level 2000mg/kg. OGTT was performed by oral administration of PHF with dose 200 and 400mg/kg body weight result was found to be gradually decreased in blood glucose level 75.75 ± 1.92 mg/dl and 72 ± 2.73 mg/dl at 180min from the study it was predicted that PHF possess Anti-hyperglycemic activity. Experimental study was shows that on repeated administration of PHF and glibenclamide for 14 days, a sustained and significant decrease in the average blood glucose level of diabetic rats was observed. End of the interventional period biochemical parameters were studied, and it was found to be level of SGOT and urea level remain constant at dose of 200mg/kg, decrease in SGPT is near to standard and decrease in creatinine level is greater than Std at dose of 400mg/kg.

Conclusion: PHF containing extracts of (*Azadirachta indica*, *Moringa oleifera* and *Andrographis paniculata*) showed significant antidiabetic and antihyperlipidemic activity which was close to standard drug. Along with remarkable reduction in Total Cholesterol (TC) level and increased in High Density Lipoprotein (HDL) DXM induced diabetes rats. The formulation has emerged as potential combination which can challenge the synthetic drug.

Keywords: Diabetes mellitus; *Azadirachta indica*; *Moringa oleifera*; *Andrographis paniculata*; Polyherbal formulation, Glibenclamide

INTRODUCTION

Importance of Herbal in Mankind

Herbal drugs play an important role in the development of potent therapeutic agents. Furthermore, it has proven their potential for the prevention of several ailments. Earlier human beings started their studies on diseases and its treatments, but there was no evidence found that people have prehistoric use of synthetic medicines for their sickness [1]. However, they



Design and Fabrication of Oral Fast Dissolving Film of Tramadol Hydrochloride

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ABSTRACT: -

For the preceding two decades, there has been a brightened demand for more patient-compliant dosage forms. Modern progresses in the technology have offered viable dosage substitutions from oral route for pediatric, geriatric, bedridden, nauseous or noncompliant patients. Buccal drug delivery has newly become a chief route of drug administration. Due to fast dissolution it afford sooner onset of action, sidestepping the first pass metabolism, dropping gastric degradation and metabolism of drugs and thus enhance their oral bioavailability. These properties of oral films with patient convenience and compliance made prevalent and accepted dosage form for pediatric and geriatric as well as adult residents.

Keywords: -Mouth dissolving film, Hydrophilic polymers, Formulation consideration, Manufacturing techniques, Evaluation parameters.

INTRODUCTION: -

The definitive aim of every drug conveyance system is the efficacious delivery of the drug, in which practically 90% of the drugs are directed to the body for the action of numerous sicknesses and disease as it is observed as the harmless, most suitable and most inexpensive method of drug delivery having the uppermost patient compliance. Fast dissolving oral films or oral wafers or oral strips or sublingual strips or oral thin films are the greatest forward-thinking form of oral solid dosage form due to more elasticity and coziness. [1] It progresses the usefulness of active pharmaceutical requirements by liquefying it within a minute of oral cavity after the interaction with saliva deprived of chewing and no necessity of water for administration. It provides speedy absorption and prompt bioavailability of drugs due to extraordinary blood flow and permeability of oral mucosa is 4-1000 times superior than that of skin. [2,3] Fast dissolving oral films are advantageous in patients such as pediatric, geriatrics, incapacitated, emetic patients, diarrhea, sudden period of allergic attacks or coughing for those who have an energetic life style. [4,5] The practice of such dosage form is likewise valuable whether indigenous accomplishment desired such as local anesthetic for toothaches, oral ulcers, cold sores or teething. At present, Tramadol is accessible in the form of tablet, infusion as well as capsules in the market. Some pediatric and geriatrics patients are non-cooperative with these dosage forms. [6] From now oral disintegrating films have become important tool to improve the patient compliance.

Tramadol hydrochloride is a centrally acting synthetic opioid analgesic binding to specific opioid receptors. It is castoff in the supervision of long-lasting pain and is suggested as chief line drug in the treatment of postoperative or orthopedic damage induced acute pain. The contemporary effort is planned to formulate and estimate oral fast dissolving film of tramadol hydrochloride as an innovative arrangement of continued analgesia for patients with orthopedic wounds. The drug possessions of tramadol hydrochloride are entirely appropriate on the drug selection criteria of the mouth dissolving film. Tramadol hydrochloride is fits to BCS class-I as it is having extraordinary solubility and high permeability which is tolerable for preparation of mouth dissolving film.

ANATOMY OF ORAL CAVITY: -

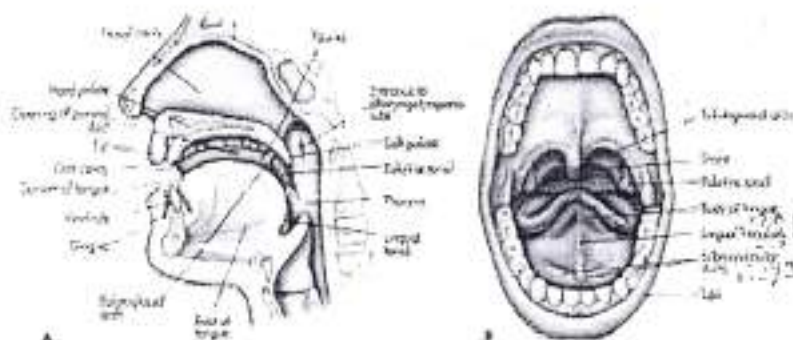


Fig 1:- Anatomy of oral cavity

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Synthesis, Analgesic and Anti-Inflammatory Activities of Some Pyrazolo[3,4-c]Pyrazole Derivatives

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Abstract—Historically, heterocyclic compounds containing Nitrogen, and their derivatives have been invaluable as a source of therapeutic agents. Pyrazole, with two nitrogen atoms and aromatic character, provides diverse functionality and stereochemical complexity in a five-membered ring structure. In Knorr pyrazole synthesis, diimine compound gets deprotonated to regenerate the acid catalyst and provide the final pyrazole product. Formation of pyrazole derivatives from hydrazines, hydrazides, semicarbazides, thiosemicarbazide and aminoguanidines by condensation with 1,3-dicarbonyl compounds is possible. As fused pyrazoles are reported to be well known pharmacophores, this has motivated to synthesize some of the pyrazolopyrazole derivatives by using hydrazine hydrate, thiosemicarbazide and semicarbazide. A series of 3-(aryl)-4-methyl-3a,6-dihydropyrazolo[3,4-c]pyrazole-2(3H)-carboxamides (IVa3-e3), 3-(aryl)-4-methyl-3a,6-dihydropyrazolo[3,4-c]pyrazole-2(3H)-carbothioamide (IVa2-e2) and 4-(aryl)-3-methyl-1,3a,4,5-tetrahydropyrazolo[3,4-c]pyrazoles (IVa1-e1) were synthesized by conventional method where fused pyrazolopyrazoles were prepared. All the compounds were synthesized with good yield (56-81 %) and characterized by IR, ¹H NMR spectral data and C, H, N elemental analysis. All the synthesized compounds exhibited analgesic and anti-inflammatory activities.

Keywords—analgesic, anti-inflammatory, knorr pyrazole synthesis, pyrazole, pyrazolo[3,4-c]pyrazole.

Introduction

Pyrazole refers to the significant [1] class of simple aromatic ring organic compounds of the heterocyclic series characterized by a 5-membered ring structure composed of three carbon atoms and two nitrogen atoms in adjacent positions [2-4]. Being so composed and having pharmacological effects on humans, they are classified as alkaloids, although they are rare in nature. In 1959, the first natural pyrazole, 1-pyrazolyl-alanine, was isolated from seeds of watermelons. Nitrated-pyrazole-based energetic compounds have attracted wide publicity in the field of energetic materials [5]. The term

pyrazole was given by Ludwig Knorr in 1883. Researchers synthesized pyrazole scaffold and studied their applications in Alzheimer's Disease and Parkinson's Disease Treatment [6]. Formation of pyrazole derivatives from hydrazines, hydrazides, semicarbazides and aminoguanidines by condensation with 1,3-dicarbonyl compounds is possible. Pyrazole derivatives have a long history of application in agrochemicals and pharmaceutical industry as herbicides and active pharmaceuticals. Thienopyrazole Moieties are also proved effective [7]. Pyrazoles have been the recent target of numerous methodologies, mostly due to their prevalence as scaffolds in drug discovery programs as antimicrobials [8-9] as HMG-CoA reductase inhibitors, as inhibitors of HIV-1 reverse transcriptase and synthesis in particular of bioactive compounds and reactions in different media. The pyrazole ring is present as the core in a variety of leading drugs such as Celebrex, Viagra or Rimonabant. Pyrazoles are found to possess anti-inflammatory [10-11] and analgesic [10, 12] activities. Many attempts were made by researchers to find out able potent pyrazolo-pyrazole derivatives [13-16] and applications [17] of pyrazoles and related compounds to enhance the biological activity.

Materials and Methods

Well dried apparatus was used to conduct the reactions requiring anhydrous conditions. Laboratory reagent grade solvents and reagents used and purified by distillation and crystallization wherever necessary. Open capillary method was used for determining melting points of newly synthesized compounds. The final products were purified by recrystallization and purity was checked by micro TLC.

The IR spectra of the compounds were recorded on JASCO FT/IR-5300 spectrometer using KBr pressed pellet. ¹H NMR spectra were recorded in a BRUKER DPX-200MHz spectrometer using TMS as internal standard. Perkin Elmer 2400 elemental analyzer was used for analysis of C, H and N which were found within ± 0.4 % of the theoretical values.



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Comparative evaluation of phytochemical constituents by GC-MS and antitubercular & antimicrobial potential of *Ceiba pentandra* and *Parmotrema perlatum* against resistant strains

Authors

G.Swaruparani³ and M. Vijaya Jyothi² K. Varalakshmi Devi¹, E. Bhargav²

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2021/7/5

Journal

Journal of Pharmaceutical Research International

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Description

Ceiba pentandra and *Parmotrema perlatum* lichen are two illustrious spices. Apart from their benefit as aromas, These are known for various therapeutic activities. Both are well known as appetizers. Decoctions of these powders are used to relieve cough, anorexia and helminthiasis etc. Though several studies on antimicrobial activities of these two plants are available, studies on resistant microorganisms and anti tubercular activity are very limited. Hence, the author made an attempt to identify the phytochemical constituents present in methanolic and n-


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GyrB inhibitors as potential antibacterial agents: a review

Authors

Swarupa Rani Gurram, Mohammed Afzal Azam

Publication date

2021/7

Source

Monatshefte für Chemie-Chemical Monthly

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Description

Bacterial resistance to antibiotics is rising to dangerously high levels globally making it one of the most urgent public health problems. Hence, there is an urgent need to develop new and potent antibacterial agents. ATP-dependent bacterial GyrB enzyme is crucial for the maintenance of DNA topology and survival of bacterial cells. GyrB is ubiquitous in bacterial cells but absent in human making it an attractive target for the development of antibacterial agents. Several GyrB inhibitors are described in the literature including coumarins, synthetic coumarins, triazine derivatives, benzimidazole ureas, benzothiazole ureas, pyrimidine-based analogues, pyrrolopyrimidines, 9H-pyrimido[4,5-*b*]indoles, thiazole-aminopiperidine hybrid analogue, pyrimido[4,5-*b*]indol-8-amine, aminopyrazinamide, thiazolyl pyrazole carboxamides, 3-(thiazol-2-yl)-1*H*-indazole derivatives, natural flavonoid quercetin and phytotoxin ...


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Original Paper | [Published: 14 June 2021](#)

Design, synthesis and biological evaluation of some novel N'-(1,3-benzothiazol-2-yl)-arylamide derivatives as antibacterial agents

[Swarupa Rani Gurram](#) & [Mohammed Afzal Azam](#)

Chemical Papers **75**, 5435–5452
(2021) | [Cite this article](#)

239 Accesses | **2** Citations | [Metrics](#)

Abstract

In the present work, we carried out hydroxybenzotriazole (HOBT) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDCl)-mediated synthesis of new N'-(1,3-benzothiazol-2-yl)-arylamides C₁₋₁₈ in high yields under relatively

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Design, Synthesis, antibacterial evaluation and molecular docking studies of some newer benzothiazole containing aryl and alkaryl hydrazides

Authors

Swarupa Rani Gurram, Mohammed Afzal Azam

Publication date

2021/7

Journal

Chemistry & Biodiversity

Volume

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Issue

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Description

The alarming rise of bacterial resistance is occurring worldwide and endangering the efficacy of antibiotics. Therefore, development of new and efficient antibacterial agents remains paramount. In the present work, we designed and synthesized a series of N'-(1,3-benzothiazol-2-yl)-substituted aryl/alkaryl hydrazides **C1-C27** and evaluated them *in vitro* for their antibacterial activity. Among all tested compounds, **C10**, **C15**, and **C24** showed potent activity against *Staphylococcus aureus* ATCC 43300 (MRSA). Minimum bactericidal concentration studies of synthesized compounds are performed against selected bacterial strains. Time kill kinetics showed that the compounds **C10** and **C15** possess bactericidal activity against MRSA ATCC 43300, while compound **C24** possess bactericidal activity against *S. aureus* NCIM 5022. In the

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NANOCRYSTAL DRUG DELIVERY CONQUERS THE COMPLICATIONS ASSOCIATED WITH PHARMACOKINETIC EVENTS OF ANTICANCER FORMULATIONS

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ABSTRACT

Nanotechnology has recently gained increased attention for its capability to effectively diagnose and treat various tumors. Nanocarriers have been used to circumvent the problems associated with conventional antitumor drug delivery systems, including their nonspecificity, severe side effects, burst release and damaging the normal cells. Nanocarriers improve the bioavailability and therapeutic efficiency of antitumor drugs, while providing preferential accumulation at the target site. A number of nanocarriers have been developed; however, only a few of them are clinically approved for the delivery of antitumor drugs for their intended actions at the targeted sites. Nano/crystals owing to its ability to modify the physicochemical and biological properties of the drug have gained widespread attention among the research scientists. This review provides comprehensive detail on the associated advantages, challenges, factors affecting physicochemical properties, and optimization parameters about the stability of nanocrystals. In this review, the evolution of nanocrystals is discussed as first-generation simple nanocrystals,

Method development and validation of cabozantinib by LC-MS/MS

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Abstract

The objective of this method is to be simple, precise, and systematic performed by LC-MS/MS instrument. The mass spectrometric determination was performed using electrospray ionization in the positive mode with multiple reaction monitoring (MRM) mode and precursor ion product ion transition to produce ion of m/z 362.2 > 303 for cabozantinib. The effective separation of cabozantinib was achieved 5.144g (7.3 min x 100 mm, 3.5 µl) column and the mobile phase composition is 0.2% formic acid acetonitrile (40:60 v/v) purged at 0.12 mL/min flow rate. The R_t of cabozantinib was found to be 1.34 minutes. The LOD and LOQ were found at 2.5 ng/ml and 5 ng/ml concentrations and linearly concentration were in a range of 5 ng/ml to 75 ng/ml with regression correlation coefficient of 0.999. The % RSD value of accuracy was observed at 1.2-2.8. The method validation assay was found to be 99.87%. The developed method and validation parameters were accepted as per USP38 guidelines.

Keywords

Cabozantinib, LC-MS/MS, Validation, Limit of detection, % RSD

Introduction

Cabozantinib is an anticancer drug and its molecular structure is shown in Fig. 1. The mechanism of action of cabozantinib is tyrosine kinase inhibitor (TKI) and effects on vascular permeability factor (VEGF) (Yakas FM et al. 2011). A phase 3 randomised controlled study of cabozantinib has higher progression free survival (PFS) overall survival (OS) or overall response rate (ORR) as opposed to drug effluor in patients who progressed following before vascular endothelial factor (VEGF) growing molecularly targeted drugs resulting in its accepted by USFDA (Chinnai TK et al. 2015). Cabozantinib is additionally accepted for utilization in the front line position for patients with midsize / low-risk patients (Chinnai TK et al. 2016).

Tyrosine kinase (TK) are considered possible attack for the latest drug progress mostly for cancer and rheumatoid arthritis drugs inhibitors. The past various tyrosine kinase inhibitors (TKI) have been grown and accepted for medications of different classifications of cancer with each one targeting certain sign pathways (Nguyen L et al. 2015). Moreover modern further have additional findings of the Janus kinases (JAKs) (Tolaney SM et al. 2016) which by their inhibition established a novel curative path for cancer and immunity disorders (Lacey S et al. 2015).

The heart rhythm problems including long QT interval observed in inpatient history to the drug should be used with caution (Chinnai A et al. 2012; Takeda H et al. 2017; Chinnai I et al. 2018; Van Schil PE et al. 2018; Wierand K et al. 2019; Poole and Jeanne E. 2020). Caboz-

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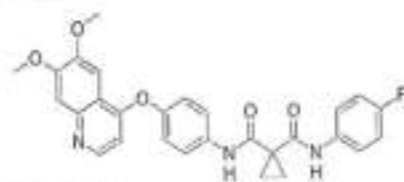


Figure 1. Shows the structure of cabozantinib

antinib and sunitinib drugs were marketed under the brand name of opitvo and used for various classifications of cancer treatment include melanoma, lung cancer, renal cell cancer, Hodgkin lymphoma, head, and neck cancer and colon cancer, and liver cancer. The usual side effects contain tiredness, rash, liver problems, muscle pain, and cough (Chinnai S et al. 2001; Chinnai A et al. 2012; Takeda H et al. 2017; Ashok Gand Mondal S 2016; Chinnai L et al. 2018; Wierand K et al. 2019).

Materials and methods

Cabozantinib standard powder and API Inactive > 99%

Preparation of standard stock solution

0.1 ml of the above standard sample solution was transferred into 10 ml of volumetric flask and diluted with methanol and the resulting solution concentration is 10 µg/ml. This solution was considered a standard stock solution.

Preparation of sample solution

10mg of cabozantinib (the pharmaceutical product powder) was transferred into 10 ml of volumetric flask and diluted with 10 ml of methanol. This solution concentration is 1000 µg/ml.

Preparation of sample stock solution

0.1 ml of the above sample solution was transferred into 10 ml of volumetric flask and diluted with methanol and the resulting solution concentration is 10 µg/ml. This solution was considered a sample stock solution.

Method validation

System suitability

Ans
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Development and Validation of RP-HPLC Method for Simultaneous Estimation of Atorvastatin and Ezetimibe in Combined Formulation

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Abstract

A simple, selective, robust and sensitive reversed phase high performance liquid chromatography method has been developed and validated for the simultaneous estimation of Atorvastatin and Ezetimibe in bulk drug and pharmaceutical formulations. The separation was achieved on a phenomenex C-18 (250 × 4.6 mm, packed with 5 μ) column by using an isocratic mobile phase mixture composed of Acetonitrile: ammonium acetate buffer pH 3.0 (50:50, v/v) with 1.1 mL/min as flow rate and the eluents were monitored at 247 nm. The retention times for Atorvastatin, Ezetimibe were 3.3, 4.5 min respectively, the linearity for both analytes was found to that $r^2 = 0.991$ and 0.986 for Atorvastatin and Ezetimibe respectively. The method was validated for its system suitability, accuracy, precision and stability. The proposed method was successfully employed for the simultaneous quantification of Atorvastatin and Ezetimibe in their pharmaceutical formulation.

Keywords

Atorvastatin and Ezetimibe

INTRODUCTION

Atorvastatin (ATR) is a synthetic lipid-lowering agent is chemically [R-(R*, R*)]-2-(4-fluorophenyl) b-dihydroxy-5-1-methyl ethyl)-3-phenyl-4-[(phenylamino)carbonyl]-1H-pyrrole-1-heptanoic acid. It lowers the cholesterol level by inhibiting the 3-hydroxy-3-methyl-glutaryl reductase (HMG-CoA reductase) coenzyme. HMG-CoA reductase is responsible for the conversion of HMG-CoA to mevalonate, an early and rate limiting step in the synthesis of cholesterol in liver. Inhibition of cholesterol synthesis in the liver leads to an increase in LDL catabolism. This also reduces the LDL-

production to some extent which results in inhibition of hepatic synthesis of very low density lipoprotein, the precursor of LDL-cholesterol.¹⁻² There are numerous methods for estimation atorvastatin alone HPLC and in combination with other drugs such as ramipril, aspirin, telmisartan, fenofibrate were reported³⁻⁴. Ezetimibe (EZT) is chemically 1-(4-fluorophenyl)-3(R) [3-(4-fluorophenyl)-3(S)-hydroxypropyl]-4(S) (4hydroxyphenyl)-2-azetidione] is also a lipid lowering agent. It reduces the blood cholesterol by preventing intestinal absorption of cholesterol without altering absorption of triglycerides, fatty

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**METHOD DEVELOPMENT AND VALIDATION FOR SIMULTANEOUS ESTIMATION OF
TELMISARTAN AND ATORVASTATIN BY RP-HPLC**Ramakrishna Reddy Voggu^{1*}, Ravi Teja, Tumburu², M. Kishore³^{1*}Department of Chemistry, Cleveland State University, Cleveland, OH 44115, USA.²MSN Laboratories Pvt.Limited, Telangana.³Department of Pharmaceutical Analysis, Pratishtha Institute of Pharmaceutical Sciences, Suryapet Telangana.

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ABSTRACT

The present work describes a simple, rapid, and reproducible reverse phase high performance liquid chromatography (RP-HPLC) method for the simultaneous estimation of Telmisartan and Atorvastatin. C18 column chromatography (RP-HPLC) method for the simultaneous estimation of Telmisartan and Atorvastatin. C18 column (Inertsil-Extend C₁₈ (250 × 4.6 mm, packed with 5 μm) and a mobile phase containing Buffer: ACN, 40:60 v/v mixtures was used for the separation and quantification. The flow rate was 0.8 mL/min and the eluents were detected by UV detector at 250 nm. The retention times were found to be 2.766 and 5.383 mins, respectively. The developed method was validated according to ICH guidelines Q2 (R1) and found to be linear within the range of 10-100 μg/mL for both drugs. The developed method was applied successfully for assay of Telmisartan and Atorvastatin in their combined in-house developed dosage forms and *in vitro* dissolution studies.

KEYWORDS: Telmisartan, *in vitro*, Atorvastatin, liquid chromatography (RP-HPLC).**1. INTRODUCTION**

Telmisartan blocks the vasoconstrictor and aldosterone-secreting effects of angiotensin II by selectively blocking the binding of angiotensin II to the AT₁ receptor in many tissues, such as vascular smooth muscle and the adrenal gland. Telmisartan does not bind to or block other hormone receptors or ion channels known to be important in cardiovascular regulation.

Atorvastatin selectively and competitively inhibits the hepatic enzyme HMG-CoA reductase. As HMG-CoA reductase is responsible for converting HMG-CoA to mevalonate in the cholesterol biosynthesis pathway, this result in a subsequent decrease in hepatic cholesterol levels. Decreased hepatic cholesterol levels stimulates up regulation of hepatic LDL-C receptors which increases hepatic uptake of LDL-C and reduces serum LDL-C concentrations.

2. EXPERIMENTAL DESIGN

2.1. Chemicals and Reagents: Telmisartan (94.43%) and Atorvastatin calcium (94.64%) were obtained from the Dr. Reddys laboratories, Hyderabad, India, and Biocon limited, Bangalore, India respectively as gift samples. Water HPLC Grade, acetonitrile HPLC Grade, Ortho phosphoric acid (AR grade) and other reagents of HPLC grade were procured from Merck. Tablets (Telistaplus 40) were purchased from Indian market containing 40mg Telmisartan and 10mg atorvastatin calcium per tablet.

2.2. HPLC Instrumentation and Conditions:

Quantitative HPLC was performed on an Younglin Acme 9000 High pressure liquid chromatographic instrument for the analysis. The instrument is provided with solvent delivery module with UV-detector and Inertsil extended, ODS Reverse phase column (250mm × 4.6mm and 5μ particle size). Manual injector and window based Autochro 3000 software was used for its recording and analysis. A Sartorius electronic balance was used for weighing the materials. Uv/vis double beam spectrophotometer SL 160 with "Spectra Treats" software.

2.2.1. Selection of mobile phase:

Pure drug of Telmisartan and Atorvastatin calcium of mixed standard stock solution (40μg/ml of telmisartan and 10μg/ml of atorvastatin calcium) were taken and 20μl sample was injected in to RP - HPLC system and run in different solvent systems. Different mobile phases systems like Acetonitrile: Water, Methanol: water, Acetonitrile: Phosphate buffer were tried in order to determine the best conditions for the effective separation of telmisartan and atorvastatin calcium. The mobile phase consisting of acetonitrile and potassium dihydrogen Phosphate buffer, pH is adjusted to 3.5±0.03 in the ratio of (60:40% v/v) was selected as it gave high resolution for telmisartan and atorvastatin calcium with minimal tailing.

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Method Development and Validation for Simultaneous Estimation of telithromycin and Ketoprofen by RP-HPLC

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ABSTRACT

The present work describes a simple, rapid, and reproducible reverse phase high performance liquid chromatography (RP-HPLC) method for the simultaneous estimation of telithromycin (TLM) and ketoprofen (KP). C18 column (chromosil ODS, 4 μ m, 200 \times 4.0mm) and a mobile phase containing phosphate buffer (0.05 M) along with 1-octane sulphonic acid sodium salt monohydrate (0.005 M) adjusted to pH 3.2: acetonitrile (45 : 55 v/v) mixture was used for the separation and quantification. The flow rate was 0.8 mL/min and the eluents were detected by UV detector at 225 nm. The retention times were found to be 3.48 and 5.42 mins, respectively. The developed method was validated according to ICH guidelines Q2 (R1) and found to be linear within the range of 75–175 μ g/mL for both drugs. The developed method was applied successfully for assay of telithromycin and ketoprofen in their combined in-house developed dosage forms and *in vitro* dissolution studies.

Keywords: Telithromycin, Ketoprofen, Chromosil

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DEVELOPMENT AND VALIDATION OF RP-HPLC METHOD FOR QUANTITATIVE ESTIMATION OF ARMODAFINIL IN BULK DRUG AND ITS PHARMACEUTICAL DOSAGE FORM

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ABSTRACT


The objective of the present study was to develop and validate a novel RP-HPLC method for determination of Armodafinil in pharmaceutical dosage form. Chromatographic separation was conducted on Shimadzu-2010 with the quaternary pump, Symmetry-C₈ column (4.6 mm I'd. X 150 mm, 5 μm particle sizes) and with photodiode array detector. Mobile phase consisted of Buffer and Methanol were mixed in the ratio of 40:60 v/v, was used at a flow rate of 1.0 ml/min and detection wavelength was set at 225 nm. The retention time for Armodafinil was found to be 3.20 min. The calibration was linear ($r^2=0.998$) in the concentration range of 25 to 150 μg/ml. The limit of detection and the limit of quantitation were found to be 0.6812μg/ml and 1.9500μg/ml respectively. Recovery of Armodafinil in tablet

formulation was observed in the range of 99.67- 101.80%. Percentage assay of Armodafinil was found to be 99.71% w/w. Thus the novel proposed method for Armodafinil was found to be feasible for the estimation of Armodafinil in bulk as well as a pharmaceutical dosage form.

KEYWORDS: Armodafinil, RP-HPLC, Validation, ICH guidelines.

INTRODUCTION

Armodafinil is a wakefulness-promoting agent for oral administration, enantiomer of Modafinil which is a mixture of the R and S- enantiomers. Chemically, it is 2-


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Method development and validation of paracetamol in bulk and tablet formulation by UV-Visible spectroscopy

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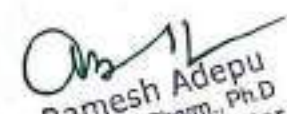
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ABSTRACT


A rapid, simple, selective and precise UV-Visible Spectrophotometric method has been developed for the determination of Paracetamol in bulk forms and solid dosage formulations. The spectrophotometric detection was carried out at an absorption maximum of 200 nm using methanol as solvent. The method was validated for specificity, linearity, accuracy, precision, and robustness. The detector response for the Paracetamol was linear over the selected concentration range 1 to 7 $\mu\text{g/ml}$ with a correlation coefficient of 0.999. The accuracy was between 99.92 & 100.94%. The precision (R.S.D.) among six sample preparations was 0.30% (Intraday) & 0.59% (Interday). The LOD and LOQ are 0.480 and 1.457 $\mu\text{g/ml}$, respectively. The recovery of Paracetamol was about 100.264%. The results demonstrated that the excipients in the commercial tablets did not interfere with the method and can be conveniently employed for routine quality control analysis of Paracetamol in bulk drug, marketed tablets and other formulations.

Keywords: Paracetamol, Spectrophotometric and ICH Guidelines


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DESIGN AND EVALUATION OF COMPRESSION COATING PULSATILE DRUG DELIVERY SYSTEM WITH NATURAL AND SYNTHETIC POLYMERS

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Research Art

DESIGN AND EVALUATION OF COMPRESS PULSATILE DRUG DELIVERY SYSTEM WITE SYNTHETIC POLYMERS

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ABSTRACT

Aim of the present work is to formulate controlled pulsatile drug delivery system chronotherapeutic approach for the treatme

PAPER

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Larvicidal and histopathological efficacy of cinnamic acid analogues: a novel strategy to reduce the dengue vector competence

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Background: A novel strategy such as conjugation of amino, Schiff's bases, and thiazole moieties to the cinnamic acid nucleus has been adopted in this study to discover new molecules that target the dengue envelope protein (DENVE). **Aim:** Among the different domains of dengue virus envelope protein (PDB ID 1OKE), we have selected a ligand-binding domain for our structure-based drug design. The designed compounds have also been docked against DENVE protein. **Methodology:** Based on the *in silico* results and synthetic feasibility, three different schemes were used to synthesize twenty-three novel cinnamic acid derivatives. Sci-finder ascertained their novelty. The synthesized derivatives were consistent with their assigned spectra. The compounds were further evaluated for their larvicidal activity and histopathological analysis. Multiple linear regression analysis was performed to derive the QSAR model, which was further evaluated internally and externally for the prediction of activity. **Results and discussion:** Four compounds, namely CA 2, CA 14, ACA 4, and CATD 2, effectively showed larvicidal activity after 24, 48, and 72 h exposure; particularly, compound CA2 showed potent larvicidal activity with LC₅₀ of 82.15 $\mu\text{g ml}^{-1}$, 65.34 $\mu\text{g ml}^{-1}$, and 38.68 $\mu\text{g ml}^{-1}$, respectively, whereas intermittent stages, causes of abscess in the gut, and siphon regions were observed through histopathological studies. **Conclusion:** Our study identified some novel chemical scaffolds as effective DENVE inhibitors with efficacious anticipated pharmacokinetic profiles, which can be modified further.

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1. Introduction

The primary carrier of viruses that cause dengue fever, *Aedes aegypti*, is found in vast areas of the tropics and subtropics. There are currently no known therapies for dengue fever. However, standard fever treatment is available (nursing care, fluid balance, electrolytes, and blood clotting parameters). As a result, the only way to reduce the prevalence of this disease is by mosquito management, which involves interrupting the disease propagation cycle by attacking mosquito larvae at breeding sites. Besides vector control, a recently authorized dengue vaccine immunizes against all four serotypes. Dengvaxia is Sanofi Pasteur's (Paris, France) chimeric yellow fever-

dengue-tetravalent dengue vaccine (CYD-TDV), the first and only of its type, and has been registered for use in 19 countries but is only available in 10.2 of them. In addition, several phase II and phase III trials have resulted in specific vaccine restrictions, such as CYD TDV being delivered exclusively to those who have previously been infected with dengue and live in endemic regions.^{1–16}

Presently around the world, dengue is endemic in 112 countries.^{1,2} Mostly in tropical and subtropical areas, each year, 50–100 million individuals are infected with DENV, resulting in nearly 500 000 severe life-threatening illnesses and 25 000 deaths.^{3,4} One attractive approach could be the interruption of the virus replication at an early stage of attachment.⁵ DENV enters the cell by receptor-mediated endocytosis followed by viral E protein-mediated membrane fusion. Membrane fusion is a major molecular event during viral entry into the host cell.⁶ E (envelope) protein is a significant component of the virion surface, plays an essential role in binding to the host receptor, and assists virus fusion.⁷ Among the three domains present in the E protein, the hinge region movement of domains I and II facilitates the fusion process.⁸ Upon lowering the pH, the E protein undergoes significant conformational changes in the hinge region, springing upwards to bring the fusion peptide closer to the host membrane for fusion to occur. Small

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Simultaneous Determination of Dolutegravir and Lamivudine in Human Plasma by LC-MS/MS

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Abstract: A rapid, simple, sensitive and selective LC-MS/MS method has been developed and validated for quantification of the Dolutegravir and Lamivudine in plasma samples. The analytical procedure involves a liquid-liquid extraction method using Emtricitabine as an internal standard (IS). The precision and accuracy data have to fulfill the requirements for quantification of the analytes in biological matrices to generate data for bioequivalence and bioavailability investigations. The chromatographic separation was achieved on a Hypurity Advance (4.6, 50 mm, 5 μ) column using a mobile phase consisting of 0.1% formic acid buffer-acetonitrile (20:80, %v/v) at a flow rate of 0.8 mL/min. The API-4000 LC-MS/MS was operated in the multiple-reaction monitoring mode using electrospray ionization. The total run time of analysis was 3 min and elution of Dolutegravir, Lamivudine and Emtricitabine (IS) occurred at 1.06, 1.84 and 0.92 min, respectively. A detailed validation of the method was performed as per the US Food and Drug Administration guidelines. The method was validated in terms of linearity, accuracy, precision, specificity, limit of detection and limit of quantitation. The standard curves found to be linear in the range of 0.10–30.0 ng/mL for Dolutegravir and 20.2–6026 ng/mL for Lamivudine, with a coefficient of correlation of ≈ 0.99 for both the compounds. Dolutegravir and Lamivudine were found to be stable in a plasma stability studies, viz. bench-top, autosampler, re-injection, wet-extract and repeated freeze-thaw cycles. The coefficient of variation was $\approx 15\%$ for intra- and inter-batch assays. The assay is suitable for pharmacokinetic study samples as demonstrated by its specificity, precision, accuracy, recovery, and stability characteristics.

Keywords: Dolutegravir and Lamivudine; Emtricitabine; plasma; Method validation; LC-MS/MS; Pharmacokinetics


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Simultaneous Determination of Dolutegravir and Lamivudine in Human Plasma by LC-MS/MS

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Abstract: A rapid, simple, sensitive and selective LC-MS/MS method has been developed and validated for quantification of the Dolutegravir and Lamivudine in plasma samples. The analytical procedure involves a liquid-liquid extraction method using Emtricitabine as an internal standard (IS). The precision and accuracy data have to fulfill the requirements for quantification of the analytes in biological matrices to generate data for bioequivalence and bioavailability investigations. The chromatographic separation was achieved on a Hypurity Advance (4.6, 50 mm, 5µ) column using a mobile phase consisting of 0.1% formic acid buffer-acetonitrile (20:80, %v/v) at flow rate of 0.8 mL/min. The API-4000 LC-MS/MS was operated in the multiple-reaction monitoring mode using electrospray ionization. The total run time of analysis was 3 min and elution of Dolutegravir, Lamivudine and Emtricitabine (IS) occurred at 1.06, 1.84 and 0.91 min, respectively. A detailed validation of the method was performed as per the US Food and Drug Administration guidelines. The method was validated in terms of linearity, accuracy, precision, specificity, limit of detection and limit of quantitation. The standard curves found to be linear in the range of 0.10–30.0 ng/mL for Dolutegravir and 20.2–6026 ng/mL for Lamivudine, with a coefficient of correlation of =0.99 for both the compounds. Dolutegravir and Lamivudine were found to be stable in a plasma stability studies, viz. bench-top, autosampler, re-injection, wet-extract and repeated freeze-thaw cycles. The coefficient of variation was =15% for intra- and inter-batch assays. The assay is suitable for pharmacokinetic study samples as demonstrated by its specificity, precision, accuracy, recovery, and stability characteristics.

Keywords: Dolutegravir and Lamivudine; Emtricitabine; plasma; Method validation; LC-MS/MS; Pharmacokinetics

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Development And Validation Of Sensitive LC-MS/MS Method For Determination Of Doravirine In Human Plasma Samples

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Abstract: Doravirine is a non-nucleoside reverse transcriptase inhibitor for use in the treatment of HIV/AIDS. A simple, rapid and sensitive liquid chromatography with tandem mass spectrometry (LC-MS/MS) assay method has been proposed for the determination of Doravirine in human plasma samples using Delavirdine as internal standard (IS). Analyte and the IS were extracted from the 100 µL of K2 EDTA human plasma by Solid Phase extraction (SPE). The chromatographic separation was achieved on a Zodiac C18 column by using a mixture of Methanol and 0.1% formic acid buffer (85:15, v/v) as the mobile phase at a flow rate of 1.0 mL/min. The calibration curve obtained was linear ($r^2=0.99$) over the concentration range of 0.15 – 40.4 ng/mL. The Mass detection of Doravirine involves m/z -426.5 (parent) and 112.5 (product) and Delavirdine involves m/z - 457.2 (parent) and 362.1 (product) as internal standard in Positive ion mode. Method validation was performed as per FDA guidelines and the results met the acceptance criteria. The intra-day and inter-day precision (%CV) and accuracy results in three validation batches across six concentration levels were well within the acceptance limits. A run time of 2.00 min for each sample made it possible to analyze more number of samples in short time, thus increasing the productivity. The assay was found to be sensitive, selective and reproducible.

Keywords: Doravirine, Solid-Phase extraction, human plasma, Validation, LC-MS/MS.

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Development And Validation Of Sensitive LC-MS/MS Method For Determination Of Doravirine In Human Plasma Samples

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Keywords: Doravirine, Solid-Phase extraction, human plasma, Validation, LC-MS/MS.

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DEVELOPMENT AND VALIDATION FOR HIGH-PERFORMANCE MASS SPECTROMETRY METHOD FOR DETERMINATION OF BALOXAVIR MARBOXIL IN BIOLOGICAL MATRICES

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Keywords:

 Baloxavir marboxil,
 Human plasma, HPLC-ESI-MS/MS,
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ABSTRACT: The validated protein precipitation method was applied for the estimation of Baloxavir marboxil in human plasma with Oseltamivir as an internal standard (ISTD) by using HPLC-ESI-MS/MS. The chromatographic separation was achieved with 0.1% formic acid in combination with methanol (25:75 v/v) using the C₁₈ column Ascentis Express (50 mm × 4.6 mm, 2.7 μm). The total analysis time was 3 min and the flow rate was set to 0.6 ml/min. The mass transitions of Baloxavir marboxil and Oseltamivir obtained were m/z 572.6→250.3 and 313.2→269.1. The standard curve shows a correlation coefficient (r²) greater than 0.9983 with a range of 5.00-10000.00 pg/ml using the linear regression model.

INTRODUCTION: Influenza virus can rapidly spread in populations and are responsible for seasonal influenza epidemics around the world every year¹. Influenza virus infection can lead to serious and fatal outcomes, especially in elderly or immunocompromised patients². Although, influenza vaccination represents the key option for preventing influenza virus infection and some strategies have been investigated to optimize immunogenicity by exploring new vaccines, vaccination doses, timing or adjuvants, its benefit in immunocompromised individuals is somewhat controversial^{3,4}. Additionally, vaccine mismatch has frequently occurred between the vaccine strain and the circulating strain⁵.

Therefore, anti-influenza drugs play an important role in the control of influenza virus infections especially for patients with or at risk of severe infection and complications.

Currently, neuraminidase (NA) inhibitors are the most widely used class of anti-influenza drugs⁶. However, the emergence of influenza viruses resistant to NA inhibitors is an issue of concern⁷. In addition, previous clinical studies have indicated that NA inhibitors must be administered within 48 hours of the onset of symptoms⁸. This is difficult to do because diagnosis is often delayed⁹. Thus, novel therapeutics that can extend the therapeutic window is needed if treatment is started from more than 48 h after the onset of symptoms. Toward this aim, the recent availability of high-quality structural information of the influenza virus RNA polymerase complex¹⁰ has led to the development of antiviral drugs that target the critical roles of the proteins involved in virus replication¹¹.

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Development and Validation of Bioanalytical Method for the Quantitative Estimation of Selexipag In Biological Matrices using LC-MS/ MS

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Abstract

The validated liquid-liquid extraction method was applied for estimation of Selexipag in human plasma with Selexipag-D6 as an internal standard (ISTD) by using LC-MS/MS. The chromatographic separation was achieved with Acetonitrile: 10mM Ammonium formate (pH-4.0) (80: 20, v/v) using the CORTECS C18 COLUMN (100 x 4.6 mm, 2.7 μ). The total analysis time was 10 min and flow rate was set to 0.5 ml/min. Detection was done by turboionspray (API) positive mode with unit resolution. Quantification was by MRM, where the acquired masses for Selexipag were 498.20 \rightarrow 344.20 m/z and Selexipag-D6 was 503.70 \rightarrow 344.20 m/z. The standard curve shows correlation coefficient (r^2) greater than 0.999 with a range of 10.00-25600.00 pg/ml using the linear regression model.

Keywords: Selexipag; Human plasma; LC-MS/MS; Bioanalysis

INTRODUCTION

Pulmonary arterial hypertension (PAH) is a hemodynamic and pathophysiological condition affecting the pulmonary arterioles and characterized by progressive increases in pulmonary vascular resistance and pulmonary artery pressure, ultimately leading to right heart failure and premature death [1-3]. Recent therapeutic options have significantly improved the long-term outcome of patients with PAH, but PAH remains a disease with a poor prognosis [4-10].

Reduced expression of prostacyclin synthases in the lung and reduced levels of prostacyclin are key features of PAH. Prostacyclin is produced by endothelial cells from prostaglandin H₂ (PGH₂) by the enzyme prostacyclin synthase. Prostacyclin is a potent vasodilator and also has anti-proliferative, antithrombotic, and anti-inflammatory effects. As PAH is associated with vasoconstriction, proliferation, and thrombosis, there is a strong rationale for using prostacyclin treatment. Restoration of IP receptor signaling using prostacyclin receptor (IP receptor) agonists is an effective strategy in the treatment of the disease [11-14].

Selexipag is a novel, orally available, long acting (half-life of 6.2-13.5 h), highly selective IP receptor agonist that targets the prostacyclin pathway. Selexipag is a diphenylpyrazine derivative with a chemical structure (Figure 1) unrelated to prostacyclin and its analogues (e.g. it lacks the typical cyclopentane ring of prostacyclin analogues) [15-16].

Selexipag (Fig:1) is a selective non-prostanoid IP prostacyclin receptor agonist. The chemical name of selexipag is 2-[4-[(5,6-diphenylpyrazin-2-yl)(isopropyl)amino]butoxy]-N-(methylsulfonyl)acetamide. It has a molecular formula of C₂₆H₃₂N₄O₄S of 496.62. Selexipag is a pale yellow crystalline powder that is practically insoluble in water. In the solid state selexipag is very stable, is not hygroscopic, and is not light sensitive [17-18].

Literature review shows that UV-VIS spectroscopy [19], HPLC [20] methods were reported for determination of selexipag in pharmaceutical formulations and none of the methods were reported for determination of selexipag in biological samples by LC-MS/MS using deuterated internal standard.

The present investigation reports a simple, sensitive, precise LC-MS/MS method for the analysis of Selexipag in plasma based on the LLE with ethyl acetate. The developed method was validated as per FDA guidelines [21-23].

MATERIALS AND METHODS

Materials:

Chemical Resources

Selexipag (SP) and Selexipag-D6 (SPIS) (Fig:1.0) were procured from Hetero Pharmaceuticals, Hyderabad, India. Water (HPLC Grade), Ammonium acetate, (analytical grade) were purchased from Merck, Mumbai, India. Acetonitrile (HPLC Grade), Methanol (HPLC grade), Ethyl acetate (HPLC grade) were obtained from J.T. Baker, USA. Human plasma was procured from Clinim Blood Blank, Hyderabad. Milli Q water was taken from the in-house Milli-Q system.

Instrument Resources

An API 4000 HPLC-ESI-MS/MS system (Applied Biosystems), 1200 Series HPLC system (Agilent Technologies, Waldbronn, Germany), data acquisition and processing were accomplished using Analyst® Software 1.4.1.

Methods:

Chromatographic conditions

The chromatographic separation was achieved with 0.1% formic acid in combination with acetonitrile (50:50 v/v), gave the best peak shape and low baseline noise was observed using the CORTECS C18 COLUMN (100 x 4.6 mm, 2.7 μ). The total analysis time was 10 min and flow rate was set to 0.5 ml/min. The temperature was set to 40°C for the column oven. The sample volume for the

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Reliable Mass Spectrometry Based Method For Quantitative Analysis Of Tecovirimat

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Abstract: Tecovirimat prevents viral egression from the cell by inhibiting protein P37 or its ortholog in orthopox viruses. This results in blocking viral dissemination in hosts. A simple, specific, sensitive LC/MS/MS method for the quantization of Tecovirimat in spiked plasma with Penciclovir as an internal standard by using UPLC-ESI-MS/MS. The chromatographic separation was achieved with 10 mM Ammonium acetate buffer (pH 4.0): Methanol: Acetonitrile (20:40:40% v/v/v) using the CORTECS C18, 90 Å, 2.7 µm, 4.6 mm X 150 mm analytical column. The total analysis time was 4.0 min and flow rate was set to 0.5 ml/min. The mass transitions of Tecovirimat and Penciclovir obtained were m/z 377.1/188.1 and 254.1/152.1. The method was fully validated for its sensitivity, selectivity, accuracy and precision, matrix effect, recovery, and stability. The curve indicates correlation coefficient (r^2) was superior than 0.998 with linear range of 0.03-48.0 ng/mL. The intra- and inter-day precision and relative error were all within 10%. Despite achieving high mean recovery (>80%), no interference peaks or matrix effects were observed. An accurate and reproducible novel bio-analytical method was fabricated for estimation of Tecovirimat in plasma samples by UPLC-ESI-MS/MS will be used for regular analysis and appropriate for therapeutic drug monitoring. The method permits laboratory scientists with access to the appropriate instrumentation to perform rapid Tecovirimat determination.

Keywords: Tecovirimat; Spiked human plasma; UPLC-ESI-MS/MS; Bioanalysis.

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DEVELOPMENT AND VALIDATION FOR HIGH-PERFORMANCE MASS SPECTROMETRY METHOD FOR DETERMINATION OF BALOXAVIR MARBOXIL IN BIOLOGICAL MATRICES

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Keywords:

Baloxavir marboxil,
Human plasma, HPLC-ESI-MS/MS,
Bioanalysis

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Reliable Mass Spectrometry Based Method For Quantitative Analysis Of Tecovirimat

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Method Development, Validation and Degradation Studies of Imatinib Mesylate by UPLC

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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ABSTRACT

Background: A simple, reliable and economical method was used for the study of imatinib mesylate. The optimized chromatographic conditions were determined by using a C18 intersil ODS (250 X 4.6 mm X 5 μ m) and a mobile phase containing phosphate buffer (pH 3.0): Acetonitrile: Methanol (40:30:30) v/v was pumped at 1 ml/min flow rate. The injected sample volume is 20 μ l and the analytes were eluted at 254 nm.

Results: The Retention time of imatinib mesylate was 3.503 minutes. The system suitability percentage RSD of imatinib mesylate is 0.27. The Assay of imatinib mesylate was found to be 99.37%. The imatinib mesylate LOD, LOQ values of were found to be 0.901 and 2.73 μ g/ml. Regression equation was found to be $y = 96.59x + 10.76$ form linearity calibration graph. Imatinib mesylate was degraded in acid and peroxide stress conditions, and no degradation was obtained in base, photolytic and thermal conditions.

Conclusion: The reliable UPLC method validation data observed that which can be used for analyzing routine quality control. The method is economical due to the run time is reduced, which can be used in regular quality control tests in the industry.

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REVIEW ARTICLE

A Review: Method Development Validation and Degradation Studies of some Anticancer Drugs

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ABSTRACT:

This article reviews the various analytical methods reported so far in the literature for the determination of stability and impurity profile the lenalidomide and palbociclib anti cancer drugs in single or combination with other drugs in bulk, pharmaceutical dosage forms, biological fluids, stability indicating and impurity profiling methods. The analytical methods used for the estimation of lenalidomide and palbociclib anticancer drugs reviewed in this paper includes ultraviolet spectrophotometry, high performance liquid chromatography (HPLC), ultra performance liquid chromatography (UPLC), liquid chromatography-mass spectrometry (LC-MS) and electrophoresis. This review focus on the effect of all chromatographic parameters so as to provide as fast, reliable and cost effective methodology of testing. Method development is the process of proving that analytical method is acceptable for use to measure the concentration of active pharmaceutical ingredient in a specific compound dosage form which must be validated to provide reliable data for regulatory submissions. This reviewed is mainly on analytical method development and validation, stability indicating methods, simultaneous estimation methods and bioanalytical methods. The review covers the time period from 2007 to 2019 during which analytical methods including all types of spectrophotometric and chromatographic techniques were reported. The Review covers lenalidomide and palbociclib API and formulation analytical and bioanalytical methods.

KEYWORDS: Lenalidomide, Palbociclib, High performance liquid chromatography, Liquid chromatography-mass spectrometry, validation.

INTRODUCTION:

Cancer is defined as a 'group of diseases characterized by the uncontrolled growth and spread of abnormal cells' and is one the deadliest diseases globally. Cancer represents the second most common cause of death in Europe and USA after cardiovascular diseases according to cancer facts and figure of 2016, a publication distributed by the American cancer society¹, and data extracted in October 2016 from euro stat-statistics explained web.

Albeit huge advances are being made against malignant growth, this infection stays a key general wellbeing concern and a colossal weight on European and American social orders². Every year the American culture gathers and aggregates the latest observation and the study of disease transmission information about malignant growth. In 2017, 1,688,780 new disease cases will rise and 600,920 malignant growth passings are anticipated to happen in United States³. As of late, masculine advances have been made in the improvement of surgeries, radiotherapy and chemotherapeutic agents⁴ including the instance of joining chemotherapy and agreement treatment with immunotherapy⁵.

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Method Development and Validation of Degradation Studies of Palbociclib by RP-HPLC

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ABSTRACT

Background: A simple, economical, authentic, and faithful method was used for the study of palbociclib. The Chromatographic analysis was performed by using a C18 intersil ODS (250 X 4.6 mm, 5µm) and a mobile phase containing 0.5M Ammonium acetate: Acetonitrile (40:60) v/v was passed throughout the column maintained at a temperature of 25 °C with a flow rate of 1 ml/min. Approximately, 10 µL of drug solution was injected and the analytes were eluted at 266 nm.

Results: The Retention time of palbociclib was 4.813 minutes. The system suitability percentage RSD of palbociclib is 0.11%. The Assay of palbociclib was found to be 98.85%. LOD, LOQ values of palbociclib were found to be 4.87 & 14.77 µg/ml, respectively. Regression equation of palbociclib was found to be $y = 71068x + 33776$. Palbociclib was found to be get degraded in peroxide stress conditions, while no degradation was observed in acid, base, photolytic and thermal conditions. All verification parameters are within the range according to the ICH guidelines, and the degradation products are also within the limits, which shown that the method is stable.

Conclusion: The HPLC method development and validation data shown that this is a reliable method which can be used for analyzing regular quality control. The proposed HPLC method was found to be specificity, linearity, precision, intermediate precision, and accuracy. In the currently developed RP-HPLC analytical method, the run time is reduced, which proves that the method is economical and widely acceptable, also simple and practical, which can be used in routine quality control tests in the industry.

Keywords: Palbociclib, Validation, Retention time, Degradation studies, % RSD

INTRODUCTION

Palbociclib is 6-Acetyl-8-cyclopentyl-5-methyl-2-[[5-(1-piperazinyl)-2-pyridinyl] amino] pyrido [2, 3- d] pyrimidin-7(8H)-one and molecular structure shown in figure 1. Palbociclib is a new drug used for the treatment of breast cancer. US Food and Drug Administration (FDA) has given approval for Palbociclib¹. Palbociclib is used in the first-line treatment for postmenopausal women with metastatic breast cancer that is estrogen receptor (ER) - positive and human epidermal growth factor receptor 2 (HER2) - negative². Palbociclib also acts as an inhibitor of cyclin-dependent kinases 4 and 6, which are involved in promoting the growth of cancer cell³. Palbociclib is a CDK4/6 inhibitor approved for metastatic estrogen receptor-positive breast

cancer. In addition to G1 cell cycle arrest, palbociclib treatment results in cell senescence, a phenotype that is not readily explained by CDK4/6 inhibition. In order to identify a molecular mechanism responsible for palbociclib-induced senescence, we performed thermal proteome profiling of MCF7 breast cancer cells. In addition to affecting known CDK4/6 targets, palbociclib induces a thermal stabilization of the 20S proteasome, despite not directly binding to it. We further show that palbociclib treatment increases proteasome activity independently of the ubiquitin pathway. This leads to cellular senescence, which can be counteracted by proteasome inhibitors. Palbociclib-induced proteasome activation and senescence is mediated by reduced proteasome

RESEARCH ARTICLE

Method Development and Validation of Degradation Studies of Lenalidomide by RP-HPLC

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ABSTRACT:

A simple, accurate, RP HPLC method was developed by this study determination of lenalidomide. This method is developed by Shimadzu LC -2010 HT by using C18 (250 X 4.6 X mm X 5 μ) column in solvents Phosphate buffer: Acetonitrile (55:45) v/v as mobile phase and the temperature was maintained at 25 °C. The mobile phase flow rate 1ml/min was pumped and sample wavelength was detected at 242 nm by ultraviolet -visible spectrophotometer. The retention time was found 2.5 min. The number of theoretical plates and tailing factor for lenalidomide was observed 16199.817 (NLT 2000) and 1.128 (NMT 2). The method was validated for analytical standards such as linearity, accuracy, precision, system suitability and robustness. LOD and LOQ values obtained from regression of lenalidomide 0.058 and 0.174 μ g/ml. The regression equation of validated method for lenalidomide is $Y=5223x+183075$. In wide range of 25 to 150 (μ g/ml) the linearity was observed. The method was validated and a recovery study indicates accuracy of this method. The Retention time less compared to established methods. The method was validated by determining its accuracy, precision and system suitability. The results of the study showed that the proposed RP-HPLC method is simple, rapid, precise and accurate, which is useful for the routine determination of Lenalidomide in bulk drug and in its pharmaceutical dosage forms.

KEYWORDS: Lenalidomide, High performance liquid chromatography, Mobile phase, Validation, Degradation.

INTRODUCTION:

Lenalidomide is a derivative of thalidomide with better biological activity. Lenalidomide chemically it is 3-(4-Amino-1, 3-dihydro-1-oxo-2H-isoindol-2-yl)-2, 6-piperidinedione is represented in figure 1.

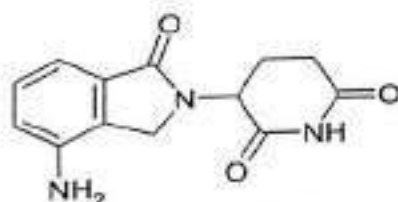


Figure 1: Chemical Structure of Lenalidomide

The chemical formula is C₁₃H₁₃N₃O₃ and molecular weight is 259.261 g/mol. Lenalidomide (LND) is an oral immunomodulatory drug with anti-angiogenic and anti-neoplastic properties. It fundamentally takes after thalidomide however has an improved danger profile and progressively strong immunomodulatory action^{1, 2}. LND showed wonderful clinical movement in treatment of numerous myeloma malady³⁻⁷ by means of a various pathways system 8-11. The system of activity of lenalidomide stays to be completely portrayed, anyway it has been exhibited that lenalidomide represses the outflow of cyclooxygenase-2 (COX-2), yet not COX-1, in vitro. In vivo it initiates tumor cell apoptosis legitimately and in a roundabout way by restraint of bone marrow stromal cell support, by hostile to angiogenic and against osteo clastogenic impacts, and by immunomodulatory action. LND shows direct pharmacokinetics in sound subjects just as in patients with ordinary renal capacity. The



Potential Coumarin Thiosemicarbazone Hybrids as BRCA-1 Mimetics for ER Positive Breast Cancer Therapy: An *In-silico* Approach

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ABSTRACT

The goal of this study is to find a novel class of BRCA-1 mimics for Estrogen Receptor α (ER α) breast cancer that works differently from conventional anti-estrogens. Breast Cancer Susceptibility Protein-1 (BRCA-1) is a protein was discovered to bind to ER α and decrease its function by a direct contact between regions inside BRCA-1's amino terminus and the carboxy terminus of ER α . A novel class of hybrids with coumate and thiosemicarbazone scaffolds was created with the premise of developing small compounds that imitate the function of BRCA-1 to down regulate the ER α and inhibit the tumor activity of breast cancer cells. Using Schrodinger 2020-2, ADMET and *in silico* molecular docking tests of the proposed hybrids were performed on the BRCA-1 binding cavity of ER α . TSCO-XIV and TSCO-III are developed hybrids that have high docking scores and good binding interactions with important residues.

Keywords: BRCA-1, Breast Cancer, Scaffold, Coumate, Thiosemicarbazone, ER alpha

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INTRODUCTION

Cancer is the most lethal disease, and researchers are working to find potential anticancer treatments. One of the most common types of cancer is breast cancers in women worldwide, both developed and developing [1]. Breast cancer accounts for 14% of all cancers in women in India. In 2018, India saw 1,62,468 new cases of breast cancer, with 87,090 deaths, according to Globocan 2020 data [2]. Expensive mortality is a result of poor diagnosis and high treatment costs. Antiestrogen therapy options are being developed since two-thirds of all breast cancers are Estrogen Receptor-positive (ER-positive). Oestrogen sensitivity in breast cancer is a unique feature of the disease that can be used to restrict development and/or prevent tumour formation. Indeed, the current therapeutic strategy for hormone-dependent breast cancer is to prevent oestrogen from acting on tumour cells in one of three ways: (a) using an antiestrogen like tamoxifen/raloxifen to prevent oestrogen from attaching to its major target ER α [3, 4, 5]; (b) using an aromatase inhibitor to inhibit oestrogen production; (c) using a pure antiestrogen like fulvestrant to lower ER α protein levels. Resistance to these contemporary

endocrine treatments, on the other hand, has a tendency to restrict their effectiveness. The BRCA1 gene controls the expression of the BRCA1 protein, which is a tumour suppressor. BRCA1 mutations in the breast cancer susceptibility gene increase the risk of breast cancer and a variety of other hormone-dependent tumour forms [6, 7]. Furthermore, in sporadic breast cancers, BRCA1 under expression is frequent (30–40%) [8–11], and one BRCA1 allele loss is seen in 46 percent of sporadic breast tumours. BRCA1 depletion or functional inactivation may have a role in the development of this kind of cancer, according to these data. In human cancers that have lost wild-type p53 function, missense mutations account for 81 percent of mutations [12].

The International Agency for Cancer Research (IARC) has thoroughly described these mutations [13]. The great majority of these mutations (95%) occur in p53's DNA binding domain, with six (hotspot) changes occurring at an unusually high rate [14]. The R175H zinc-binding mutant is the well-studied, as well as the most frequent missense p53 mutation in cancer [15]. The R175H mutation impairs

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Review Article (Mini-Review)

Review on Dengue Virus Fusion/Entry Process and Their Inhibition by Small Bioactive Molecules

(E-pub Ahead of Print)

Author(s): **Podila Naresh**, Shyam Sunder Pottabatula, Jubie Selvaraj*

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Anticancer Potential of Phytoconstituents Modulating Na⁺/K⁺ ATPase Pump; A Novel Repurposing Strategy

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Abstract

Repositioning the drugs through poly-pharmacological approaches, including cancer therapy is gaining scientific interest, as many non-cancer targeting drugs have well-established safety profile but unexplored for its potential to combat cancer. The complex heterotrimeric protein Na⁺/K⁺ ATPase (NKA) is complex. It is existing on the plasma membrane of eukaryotic cells and makes use of ATP for the maintenance of sodium and potassium transport. It has three subunits, α , β and γ . The α -subunit has four isoforms namely α_1 , α_2 , α_3 , and α_4 . One of the published studies reports that the α_1 subunit is over expressed and activated in certain malignancies like renal cell carcinoma, glioma, and melanoma. Thus, it is hypothesized that NKA has unique roles in cancer cell growth and development. For instance, Ouabain is a well-known inhibitor of NKA which is used primarily as a cardiac stimulant has also been recently reported for its potential anticancer properties in neuroblastoma cells. Consequently, the search for the molecules which has the potential to inhibit specific NKA in cancer cells gaining tremendous scientific attention. Recently perillyl alcohol has been reported for anticancer potential through NKA inhibition. Since perillyl alcohol has a cyclic ring in its structural frame, we opted the similar chemical signatures of Phyto terpenes and phytotannins of for our study. Thus, the present

study opted for scaffold repurposing strategy using *in-silico* methods to identify and screen some of the well-known phytocompounds for its possible anticancer effects by inhibiting NKA.

Keywords Repurposing, Phyto tannins, Phyto terpenes, perrilyl alcohol, Na K ATPase.

Introduction

Drug repositioning or drug repurposing is an approach is a way to deal with quickens the medication revelation process through the recognizable proof of a novel clinical use for a current medication affirmed for an alternate sign. A noteworthy issue of regular malignancy chemotherapy drugs (mainly DNA damaging agents) is famous symptoms that fundamentally decrease the quality existence of patients (1). As a large portion of non-malignant growth medications has pretty much nothing or decent reactions in humans, repositioning of non-disease drugs for anticancer treatment is viewed as a promising methodology for future anticancer medication improvement. Reliable with this view, a couple of those non-malignant growth medications are as of now under clinical examinations (for example Itraconazole, Nelfinavir, Digoxin, Riluzole, Mycophenolic corrosive and Disulfiram) against an assortment of human cancers (2, 3). Furthermore, drug repositioning altogether lessens the investigational time and cost. In

Anticancer potential of phytoconstituents


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Targeting a conserved pocket (n-octyl- β -D-glucoside) on the dengue virus envelope protein by small bioactive molecule inhibitors

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ABSTRACT

Dengue virus enters the cell by receptor-mediated endocytosis followed by a viral envelope (DENVE) protein-mediated membrane fusion. A small detergent molecule n-octyl- β -D-glucoside (β OG) occupies the hydrophobic pocket which is located in the hinge region plays a major role in the rearrangement. It has been reported that mutations occurred in this binding pocket lead to the alterations of pH threshold for fusion. In addition to this event, the protonation of histidine residues present in the hydrophobic pocket would also impart the conformational change of the E protein evidence this pocket as a promising target. The present study identified novel cinnamic acid analogs as significant blockers of the hydrophobic pocket through molecular modeling studies against DENVE. A library of seventy-two analogs of cinnamic acid was undertaken for the discovery process of DENV inhibitors. A Molecular docking study was used to analyze the binding mechanism between these compounds and DENV followed by ADMET prediction. Binding energies were predicted by the MMGBSA study. The Molecular dynamic simulation was utilized to confirm the stability of potential compound binding. The compounds CA and SCA derivatives have been tested against HSV-1 & 2 viruses. From the computational results, the compounds CA1, CA2, SCA 60, SCA 57, SCA 37, SCA 58, and SCA 14 exhibited favorable interaction energy. The compounds have *in-vitro* antiviral activity; the results clearly indicate that the compounds showed the activity against both the viruses (HSV-1 & HSV-2). Our study provides valuable information on the discovery of small molecules DENVE inhibitors.

ARTICLE HISTORY

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KEYWORDS

Dengue; dynamic acid; envelope; ADMET; docking; dynamics

1. Introduction

Dengue virus (DENV) is a virus transmitted by the flavivirus species, which includes yellow fever, West Nile, Japanese encephalitis, and Zika virus (YFV, WNV, JEV, ZIKV) respectively. Up over 390 million dengue infections occur annually, resulting in the worsening of dengue haemorrhage fever and dengue shock syndrome (Bhatt et al., 2013). We currently do not have a comprehensive vaccine or specific antiviral treatment to combat DENV, ZIKV, and many other flaviviruses infections (Campos et al., 2018; Sun et al., 2020). The geographical spread of the *Aedes* mosquito species beyond DENV & ZIKV and the recent explosive emergence of ZIKV in the Western Hemisphere have increased the need for cone-tumours that can reduce transmission and therapeutic inter-ventilation, which can lead to infectious diseases. Given the lack of efforts to target antiviral production against viral polymerases and proteases, alternative antiviral strategies to prevent infection are becoming increasingly important (Zhiyong et al., 2014). One attractive approach could be the

interruption of the virus replication at an early stage of attachment. Membrane fusion is a central molecular event during viral entry into the host cell (Roby et al., 2015). E (envelope) protein is a major component of the virion surface plays an important role in binding to the host receptor and assists virus fusion (Kampmann et al., 2006; Stiasny et al., 2011). Among the three domains present in the E protein, the hinge region movement of domains I and II facilitates the fusion process (Kampmann et al., 2006). Rearrangement and/or conformational changes in the hinge region by small molecules may interrupt the fusion process (Zhou & Madura, 2004). One major barrier to the development of antivirals targeting envelope proteins is the lack of a putative active site compatible with viral proteases and polymerases.

Over ten years back, crystallization of the DENVE (dengue virus envelope) protein with mill molar concentrations of the detergent β -octyl glucoside (β OG) empowered to (Modis et al., 2003) detect binding of a detergent atom in a pocket between domains I and II. The area of the detergent binding

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Research Article

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SYNTHESIS OF SOME DIHYDROPYRIMIDINONE DERIVATIVES AND STUDY OF THEIR ANTI-INFLAMMATORY ACTIVITY

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Keywords

Dihydropyrimidinones derivative, synthesis, toxicity study, anti-inflammatory activity study

ABSTRACT

This research revealed that the numbers of available heterocyclic compounds are mainly focused on nitrogen containing compounds, such as quinazolines, imidazoles, benzimidazole, quinoxalines, coumarins and pyrimidines etc. A mixture of substituted aldehydes (0.01 mol) like acetyl acetone (method 1) or ethyl acetoacetate (method 2), urea or thiourea (0.01 mol) and lemon juice (0.5 ml) were taken into a round bottom flask and reflux for 1 hour at 80°C under continuous stirring. After completion of the reaction the final product was recrystallized for purification. Simultaneously toxicity and anti-inflammatory activity were performed. But in case of using ethyl acetoacetate in method 2, the percentage yield was more as compare to using of acetyl acetone in method 1. So the derivatives obtained from method 2 were selected for further toxicity and anti-inflammatory activities.

INTRODUCTION

Medicinal chemistry is an applied science with fundamental roots originating from all branches of chemistry and biology. The term "pharmaceutical chemistry" is often substituted for "medicinal chemistry" where the compounding of drugs to materials useful in pharmacy commands considerable attention [1-3]. Dihydropyrimidinones are useful targets in chemical synthesis as they have been associated with a diverse range of therapeutic and medicinal properties [4-6]. The dihydro-


pyrimidinone scaffold is also found in various marine alkaloids, which have been shown to possess antiviral, antitumor, antibacterial and antioxidant activities [7-9]. In particular, the batzelladine alkaloids are known to be potent HIV gp-120-CD4 inhibitors. In general dihydropyrimidinones act as anticancer, calcium channel blockers, antibacterial, α -adrenergic receptor antagonist such as monestrol, oxomonestrol etc. Because of heterocyclic moiety these compounds producing pharmacological activity [10 - 13] as per the

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**REVIEW PAPER**ISSN:2394-2371
CODEN: IUSAJPHB**AQUEOUS MICROWAVE CHEMISTRY: NOVEL SYNTHETIC METHODOLOGY**

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ABSTRACT

Chemistry is the scientific study of interaction of chemical substances that are constituted of atoms or the subatomic particles; protons, electrons, and neutrons. Traditional chemistry involves study of interaction between substances in a chemistry laboratory using various forms of laboratory glassware. Traditional chemistry is perhaps the most established method for organizing atoms. Microwave irradiation has gained popularity in the past decade as a powerful tool for rapid and efficient synthesis of a variety of compounds because of selective absorption of microwave energy by polar molecules. Microwave reactions involve selective absorption of MW energy by polar molecules, non-polar molecules being inert to MW (microwave) dielectric loss. Microwave synthesis is facile and offers synthesis of variety of chemical compounds.

Keywords: - DNA fragmentation, DNA smearing, Free radicals, Antibiotics, Proven Antimicrobial Plant

INTRODUCTION

Antibiotics Conventional synthesis employs wide range of reactants, reagents, catalysts and solvents. The time required for completion of reaction is high and yield of products formed by this kind of synthesis is considerably low. The reactions accompanied may form non-selective

products and also the by-products formed from reactants as well as organic solvents are not so easily eliminated from the reaction mixture. Sometimes they may cause hazardous undesired effect. However traditional synthesis has its own merits and demerits.

ADVANTAGES

1. Synthesis of wide variety of molecular components and characterization using traditional tools.

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Metabolic Enzyme Inhibitory and Larvicidal Activity of Biosynthesized and Heat Stabilized Silver Nanoparticles Using *Annona muricata* Leaf Extract

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Abstract

The synthesis of silver nanoparticles (AgNPs) using *Annona muricata* (*A. muricata*) leaf extract and its larvicidal, metabolic enzyme inhibitory properties was demonstrated here. The AgNPs were synthesized and analyzed by using UV-visible spectroscopy and observed a maximum absorbance peak at 420 nm which corresponds to the AgNPs. The XRD analysis showed the 2 θ intense values (111, 200, 220, and 311) within the ranges of Bragg's reflection; Fourier transform infrared spectroscopy (FTIR) showed that AgNPs were capped with alkanes, amides, and alkenes functional groups which act as a reducing, capping, and stabilizing agent; and field emission scanning electron microscope (FESEM) and high-resolution transmission electron microscopy (HRTEM) results indicated that synthesized AgNPs were spherical in shape with the size of 20–34 nm and energy-dispersive X-ray (EDX) spectroscopy exhibited a strong signal of silver. Various concentrations of AgNPs (6, 12, 18, 24, 30 $\mu\text{g mL}^{-1}$) and aqueous leaf extract (ALE) (30, 60, 90, 120, 150 $\mu\text{g mL}^{-1}$) were evaluated, and in all the concentrations, AgNPs showed significant larvicidal properties against three different second instar larvae, when compared to ALE. ALE exhibited LC₅₀ and LC₉₀ values of (LC₅₀ 45.521 $\mu\text{g/mL}$; LC₉₀ 456.406 $\mu\text{g/mL}$) against *Ae. aegypti* followed by *An. stephensi* (LC₅₀ 61.878 $\mu\text{g/mL}$; LC₉₀ 565.309 $\mu\text{g/mL}$) and *Cx. quinquefasciatus* (LC₅₀ 68.952 $\mu\text{g/mL}$; LC₉₀ 444.512 $\mu\text{g/mL}$), and AgNPs were exhibited LC₅₀ and LC₉₀ values (LC₅₀ 3.089 $\mu\text{g/mL}$; LC₉₀ 18.467 $\mu\text{g/mL}$) against *Ae. aegypti* followed by *An. stephensi* (LC₅₀ 3.155 $\mu\text{g/mL}$; LC₉₀ 39.888 $\mu\text{g/mL}$) and *Cx. quinquefasciatus* (LC₅₀ 5.188 $\mu\text{g/mL}$; LC₉₀ 31.660 $\mu\text{g/mL}$), respectively. The *A. muricata* leaf extract-mediated AgNPs were also evaluated for the first time to identify their metabolic enzyme inhibitory activity which also showed significant results.

Keywords Silver nanoparticles · Metabolic enzyme inhibitory · Larvicidal activity · Heat stability · *Annona muricata*

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1 Introduction

Nanobiotechnology is one of the most promising areas in modern nanoscience and technology which has a great application tool for exploring darkest avenues of medical sciences in several ways like targeted drug delivery [10], imaging [12], artificial implants [23], and sensing [22] and also can fight against human pathogens and diseases [4]. This emerging area of research interlaces various disciplines of science such as physics, chemistry, biology, and material science. Though there are existing chemical and physical techniques available for the manufacturing of nanoparticles. These chemical methods contain the enormous side effects to our environment due to the usage of toxic chemicals also which is more expensive. This enhances the developing need to grow naturally benevolent procedures through green synthesis and other organic methodologies for the synthesis of nanoparticles. The

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A BRIEF REVIEW ON GLYCOMIMETICS AND THEIR PHARMACEUTICAL APPLICATIONS

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Keywords:

Glycomimetics, Glycyrrhizin, Arixtra, DC-SIGN, Relenza, Tamiflu

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ABSTRACT: This review enumerates the classification, role, and importance of carbohydrate derivatives and glycomimetics. Carbohydrates are polyhydroxy aldehydes or ketones. Carbohydrates are the most abundant dietary source of energy for all organisms. They are precursors for many organic compounds such as fatty acids and amino acids. They can participate in the structure of cell membranes and cellular functions such as cell growth, adhesion, and fertilization. Glycomimetics are the compounds of low molecular weight based on the structure of functional carbohydrates. The rational style of tiny molecule glycomimetics that exhibit improved drug-like properties like enlarged affinity, blood serum half-life, stability, and bioavailability. Currently, two successful drugs for influenza (Tamiflu, Relenza) are mimicking (Glycomimetics) the transition state of the enzymatic cleavage of the terminal N-acetyl neuraminic acid. A hopeful example is the antibody 2G12, which has been shown to neutralize HIV infectivity. The functional carbohydrates identified in these recognition processes themselves do not make good drug candidates. Rather, their bioactive conformations in their receptor sites can be empirically determined by physicochemical methods and used for the rational design of small molecule mimics (Glycomimetics) that have higher affinities and more drug-like properties of long serum half-life, metabolic stability, low toxicity, and oral bioavailability. These glycomimetics drugs are new chemical entities and provide innovative therapeutic strategies to address current unmet needs among a wide spectrum of disease applications.

INTRODUCTION: Compounds of low molecular weight based on the structure of functional carbohydrates. These molecules are called glycomimetics¹.

"The role of membrane glycol conjugates in a variety of pharmacologically relevant recognition phenomena has stimulated interest in the synthesis and biological evaluation of analogs of carbohydrates, defined as glycomimetics"².

The rational style of little molecule glycomimetics that exhibit improved drug-like properties like inflated affinity, body fluid half-life, stability, and bioavailability. Currently, two successful drugs for influenza (Tamiflu, Relenza) are mimicking (glycomimetics) the transition state of the

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RESEARCH ARTICLE

A New Class of Coumate Benzimidazole Hybrids as BRCA 1 Mimetics Through Unconventional Binding Mode; Synthesis and Preliminary Cytotoxicity Screening

Selvaraj Jubie^{1*}, Shyam Sundar P¹, Nectu Yadav¹, Podila Nares¹, Ashish Wadhvani² and Jawahar Natarajan³¹Department of Pharmaceutical Chemistry, JSS College of Pharmacy, Udhagamandalam JSS Academy of Higher Education & Research, Mysore, India; ²Department of Pharmaceutical Biotechnology, JSS College of Pharmacy, Udhagamandalam JSS Academy of Higher Education & Research, Mysore, India; ³Department of Pharmaceutics, JSS College of Pharmacy, Udhagamandalam JSS Academy of Higher Education & Research, Mysore, India**Abstract: Background:** It was found that breast cancer susceptibility protein 1 (BRCA 1) binds to estrogen receptor alpha (ER α) and inhibits its activity by direct interaction between domains within the amino terminus of BRCA 1 and the carboxy terminus of ER alpha.**Objectives:** The present work focuses to identify a new class of BRCA 1 mimetics that work differently from conventional anti-estrogens.**Methods:** A novel class of hybrids having coumate and benzimidazolone scaffolds were designed to mimic BRCA 1 protein, suppressing the tumor activity of breast cancer cells. *In silico* molecular docking studies of the designed ligands were performed on BRCA 1 binding cavity of ER alpha.**Results:** The designed hybrids which gave significant docking scores and had optimum binding interactions with key residues were selected for synthesis and *in-vitro* assay.**Conclusion:** The compounds NY1 and NY2 exhibited significant effects on suppressing MDA-MB-231 cells in the concentration of 24 μ g/ml and 44 μ g/ml, respectively.

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10.2174/157348992000191231162019**Keywords:** Breast cancer, scaffold, BRCA1, coumate, benzimidazolone, ER α .

1. INTRODUCTION

Many breast cancer therapies ultimately fail and recurrent ER alpha positive breast cancers are generally incurable due to resistance for conventional anti-estrogens [1]. Therefore, in recent years, researchers have been looking for anti-estrogens that lack their partial agonist properties and have a mechanism of action different from the existing drugs. The breast cancer susceptibility genes BRCA1 and BRCA2 are classic tumor suppressor genes that exhibit an autosomal dominant pattern of inheritance with high penetrance [2, 3]. BRCA1 carriers inherit one mutant BRCA allele and one wild-type allele; the wild-type allele is invariably deleted or mutated within the tumor^[4]. These genes function as caretakers in the maintenance of genomic stability, in part, by

participating in Homology directed DNA Repair (HDR), an error-free mechanism for the repair of Double-Strand Breaks (DSBs). Mutations of BRCA1 account for half of all hereditary breast cancers [5]; and in 30-40% of sporadic cancers, BRCA1 expression is absent or reduced, suggesting a wider role in breast cancer [6-8]. The evidence clearly states BRCA1 may regulate the response of ER alpha to its canonical ligand estradiol and inhibits by direct interaction between the amino terminus of BRCA1 and the carboxyl terminus of ER-alpha [9, 10]. Our objective is to identify a novel group of compounds that act as estrogen receptor antagonists by binding to a putative BRCA1 binding cavity that is distinct from the conventional ligand binding pocket and the co-activator binding pocket in ER α . Fig. (1).

Coumarin and benzimidazolone scaffolds suppress breast cancer cell growth [11-16], which show activity against breast cancer. In continuation of our previous study [17, 18], the present study focused on synthesizing coumarin and substituted benzimidazolone hybrids as BRCA1 mimetics which

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Drug repurposing of Daclatasvir and Fanciclovir as antivirals against dengue virus infection by *in silico* and *in vitro* techniques

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Drug repurposing is a technique for reusing an existing drug to treat another ailment. It is common knowledge that nearly all medicines used in human therapy have more than one target impact in addition to their primary action. The present work is aimed to repurpose existing antiviral drugs for dengue disease. A molecular docking study is performed with the DENVE protein for the identification of the suitable drug candidate which acts in the fusion process. For all repurposed drugs at the active site of DENVE, molecular docking experiments were performed using CLC Drug Discovery Workbench Software (PDB ID: 1OKE). The relative binding modes and the affinities of all the selected drugs were predicted and compared with the co-crystallized *n*-octyl-beta-D-glucopyranoside (β OG). The Daclatasvir (Score-53.52) makes hydrogen bonds with ALA50 and THY48. According to the docking score evaluation, the entire drug candidates had docking result ranging from -32.15 to -53.52. Among the drugs tested the two drugs namely Daclatasvir and Fanciclovir have been identified as HITS for combating DENVE protein.

Keywords: Dengue virus, Drug repurposing, Envelope protein, Hinge region, Molecular docking, *n*-Octyl-beta-D-glucopyranoside (β OG)

Dengue viral disease, a mosquito-borne viral pathogen dengue virus (DENV), has been a significant public health issue in recent decades. Dengue is currently present in 119 countries throughout the world. Fifty-hundred (50-100) million people in tropical and subtropical countries are infected with DENV per year, resulting in approximately 5,000,000 existence diseases and 25,000 deaths. DENV belongs to the Flavivirus family of the Flaviviridae family. The genome of flavivirus consists of approximately 11,000 base pairs (bp) of RNA, which translate into three structural proteins, including membrane [M], capsid [C], & envelope [E], and 7 non-structural proteins NS1, NS2A, NS2B, NS3, NS4A, NS4B, and NS5. The viral envelope consists of two transmembrane proteins, the envelope (E) and the pre-membrane (prM). E binds directly to cellular receptors and facilitates viral and cell membrane fusion through viral cell penetration and is the primary site for antibody neutralization¹.

Interruption of virus replication at the initial point of contact² can be an attractive technique. Membrane fusion is the main molecular event that occurs during the viral entrance into the host cell³. The envelope protein (E) constitutes the main component of viral surface. It is very important for fusion process through which the virus merges into host receptor⁴. Among the three domains DI, DII, and DIII present in the E protein, the migration of domains I and II in the hinge region promotes the mechanism of fusion. Rearrangement and/or conformational changes in the hinge area by small molecules can disrupt the process of fusion⁵⁻⁷.

Keeping the above facts, the present work is aimed to repurpose existing antiviral drugs for dengue disease. A molecular docking study is performed with the DENVE protein for the identification of the drug candidate which acts in the fusion process. The drugs obstructing the β OG pocket have thought to interact with conformational changes within the envelope protein that are basic for configuration. The following seven medicines were chosen based on their mechanism of action⁸ and therapeutic efficacy: Acyclovir inhibits

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Suppl. Data available on respective page of NOPR

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Dual Modulators of p53 and Cyclin D in ER Alpha Signaling by Albumin Nanovectors Bearing Zinc Chaperones for ER-positive Breast Cancer Therapy

Author(s): Shivam Sankar P., **Prabha Narish**, Justin A., Achish Wadhvani, Suresh Kumar M. and Gokulraj Jubie*

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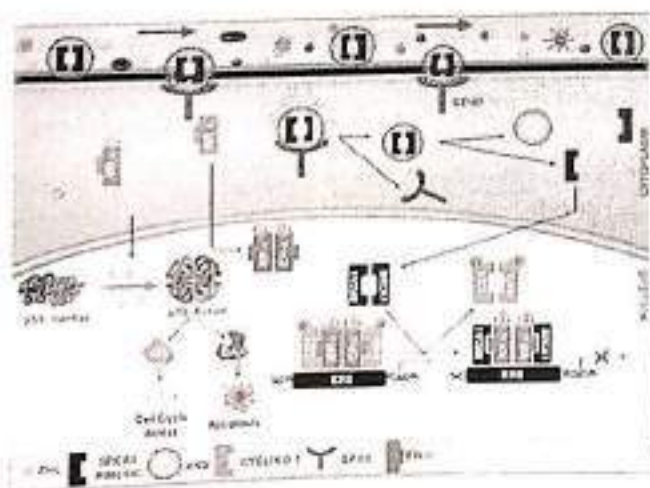


ABSTRACT

The inherited mutations and underexpression of BRCA1 in sporadic breast cancers resulting in the loss or functional inactivation of BRCA1 may contribute to a high risk of breast cancer. Recent researchers have identified small molecules (BRCA1 mimetics) that fit into a BRCA1 binding pocket within Estrogen Receptor alpha (ER α), mimic the ability of BRCA1 to inhibit ER α activity, and overcome antiestrogen resistance. Studies indicate that most of the BRCA1 breast cancer cases are associated with p53 mutations. It indicates that there is a potential connection between BRCA1 and p53. Most p53 mutations are missense point mutations that occur in the DNA-binding domain. Structural studies have demonstrated that mutant p53 core domain misfolding, especially p53-R175H, is reversible. Mutant p53 reactivation with a new class of zinc metallochaperones (ZMC) restores WT p53 structure and functions by restoring Zn²⁺ to Zn²⁺ deficient mutant p53. Considering the role of WT BRCA1 and reactivation of p53 in tumor cells, our hypothesis is to target both tumor suppressor proteins by a novel biomolecule (ZMC). Since both proteins are present in the same cell and are functionally inactive, this state may be a novel efficacious therapeutic regime for breast cancer therapy. In addition, we propose to use Albumin Nanovector (ANV) formulation for target drug release.

Keywords: Resistance, BRCA1, ER α , ZMC, albumin nanovectors, p53.

Graphical Abstract



Complete Mechanism of proposed ZMCs

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For Authorship & Reviews

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Posttranscriptional Regulation of p53 and its Targets by RNA-Binding Proteins
Chengping Liu, Xiangping Li, et al.

Multifunctional Thio-Stabilized Gold Nanoparticles for Near-Infrared Fluorescence Detection and Imaging of Activated Caspase-3

Dengue Virus Entry/Fusion Inhibition by Small Bioactive Molecules.

- **Source:** Current Trends in Biotechnology & Pharmacy . Apr2020 Suppl. p149-150. 2p.
- **Author(s):** Naresh, Podila; Jubie, S.; Girija, K.; Shyam, P.
- **Abstract:** Dengue virus enters the cell by receptor mediated endocytosis followed by viral E (envelope) protein mediated membrane fusion. Membrane fusion is a central molecular event during viral entry into host cell. E protein is a major component of the virion surface plays an important role in binding to the host receptor and assists virus fusion. Rearrangement and or conformational changes in the hinge region by small molecules may interrupt the fusion process. Among the three domains present in the E protein, Hinge region movement of domain I and II, facilitates the fusion process. Upon lowering the PH, the E protein undergoes major conformational changes in the Hinge Region springing upwards to bring the fusion peptide closer to the host membrane for fusion to occur. A small detergent molecule n-octyl- β -D- glucoside (BOG) occupies the hydrophobic pocket which is in the hinge region plays a major role in the rearrangement. It has been clearly reported that mutations within this binding pocket leads to the alterations of pH threshold for fusion. In addition to this the protonation of histidine residues present in the hydrophobic domain would also impart the conformational change of the E protein. The previously reported fusion inhibitors such as peptidic antivirals suffer from poor absorption from the gastrointestinal tract, necessitating intravenous delivery and high manufacturing costs. Keeping these views, it is proposed to design and synthesize a library of novel small bioactive molecules. Inserted at this position may have the ability to interrupt further conformational changes and hence can inhibit the fusion transition.
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Prescribing Pattern of Medications in Geriatric Patients in a South Indian Tertiary Care Teaching Hospital

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ABSTRACT

Background: Globally, the population of elderly is gradually rising. Co-morbidities and polypharmacy are the prime reasons for the inappropriate use of medications. **Objective:** A prospective, observational study was conducted in a South Indian tertiary care teaching hospital to assess the medication prescribing pattern in elderly patients and also to evaluate the inappropriateness of medications using Beer's criteria. **Materials and Methods:** Institutional ethics committee has approved the study. Written informed consent was taken from all the enrolled elderly patients meeting the inclusion criteria. Necessary demographic, clinical, laboratory and therapeutic information was collected and recorded in a suitably designed data collection form and the same was evaluated for prescribing pattern and inappropriateness using Beer's criteria. **Results:** A total of 104 patients aged above 60 years were enrolled into the study. Among them 64 patients (61.53%) were males and 40 (38.46%) were females. Among these patients 61 (58.65%) patients were in the age group of 60-65 years, 25 (24.03%) were in 66-70 years, 12 (11.53%) were in 71-75 years, 6 (5.76%) were >75 years. Common cause for hospital admission was hypertension and diabetes. As per Beer's criteria, 91.3% prescriptions given to the study patients were found inappropriate. Antibiotics and Pantoprazole were the most commonly prescribed drugs. The study findings suggest that use of poly pharmacy is high and majority medications prescribed were found inappropriate as per the Beer's criteria. **Conclusion:** Presence of clinical pharmacist would optimize the drug therapy and minimize the drug related problems and negative therapeutic outcomes in elderly patients.

Key words: Geriatrics, Beer's criteria, Inappropriate medication, Polypharmacy, Irrational prescribing.

INTRODUCTION

Geriatrics is the branch of medicine that deals with the elderly people health care.¹ Rational prescribing is defined as use of least number of medicines to obtain the best possible therapeutic outcomes in the shortest period and at an affordable cost. Prescribing Pattern Monitoring Studies (PPMS) focus on prescribing, dispensing and distribution of medicines. The main aim of PPMS is to facilitate Rational use of Medicines (RUM).² Inappropriate drug prescribing is a global problem and irrational use of drugs is becoming major concern of present-day medical practice as its consequences leading to therapy ineffectiveness, drug-related problems and increased medical expenditure.³

Five important criteria in rational drug use are accurate diagnosis, proper prescribing, correct dispensing, suitable packing, patients' adherence to their medication. Study of prescribing pattern seeks to monitor, evaluate and if necessary suggest modifications in prescribing so as to make medical care rational and cost effective.⁴ Following are the factors that affect the choice of medicines in elderly such as poly pharmacy, altered drug response, inappropriate prescribing, non-adherence to the prescribed medicines. Irrational drug use, precipitates negative therapeutic outcomes and also drains family savings.⁵

Elderly people suffer commonly from these diseases such as osteoarthritis, cardiovascular

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PHARMACOEPIDEMOLOGICAL EVALUATION OF HIV PHARMACOTHERAPY AT DISTRICT ART CENTER IN SOUTH TELANGANA

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ABSTRACT

Objective: Objective of the study was to assess the drug utilization pattern of antiretroviral drugs, and medication adherence behavior among human immunodeficiency virus (HIV) patients attending a local ART center, Suryapet, South Telangana.

Methods: This was a prospective observational study approved by institutional ethics committee. Demographic, clinical, laboratory, and the treatment details were collected on daily basis for new cases and the data add on was collected for old cases. Medication adherence behavior was assessed through Morisky Medication Adherence Scale-B.

Results: During the study period, a total of 505 HIV patients were enrolled. Among them, majority patients were women (61%), in the age group of 31-45 (49.7%), illiterates (52.6%). Major mode of transmission identified was intimate contact (74%), and majority patients were in Stage I (49%). TLD regimen was prescribed in 69.9% patients and for children the prescribed regimen was ABC, 3TC, FPV (5.1%). About 45% patients were found with medium adherence.

Conclusion: This study concludes that the most prescribed regimens were combination of TLE, and majority of the patients were found with medium adherence.

Keywords: Antiretroviral therapy, Prescription pattern, Adherence behavior, Pharmacoepidemiological survey.

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INTRODUCTION

Pharmacoepidemiology is the study of use, effects and adverse drug reactions of medication in large number of populations with the purpose of supporting the rational and cost-effective use of medications in the population to improve the desired health outcomes [1]. The human immunodeficiency virus (HIV) is a retrovirus affects the immune system, destroying or impairing their function. As the infection progress, the immune system becomes weaker, and the person becomes susceptible to infections [2]. Most advanced stage of HIV infection is called as acquired immunodeficiency syndrome (AIDS) and takes 10-15 years for an HIV-infected person to develop as AIDS case [3].

Use of HIGHLY ACTIVE ANTIRETROVIRAL THERAPY (HAART) substantially decreased death rate and translated AIDS as manageable condition. UNAIDS and WHO estimated AIDS death tolls as more than 25 million in 1981, when it was first recognized. [1] An adherence of 95% to ART is essential to achieve maximal viral suppression and minimize the opportunistic infections (OI) rate [4]. However, in clinical practice, maintenance of optimal ART adherence is challenging. A meta-analysis of 84 studies estimated that only 62% of HIV patients had achieved optimal adherence (of >90%) [5].

The present study aims at understanding prescribing patterns and medication adherence behavior of HIV patients visiting a district ART center. This helps in assessing the rational use of the antiretroviral drugs and strategies to reduce the infection rate and prolong the patient survival. Worldwide, more than twenty antiretroviral drugs belonging to Fusion inhibitors, NNRTIs, NRTIs, Chemokine receptor antagonist, Protease inhibitors, and Integrase inhibitors are licensed for formal therapy [6].

HAART is known as triple drug therapy. Studies have corroborated the combination therapy as very effective and reduce the viral load in the patients below detectable levels implying that HIV replication is

ceased [2]. In the absence of HAART, progression from HIV infection to AIDS has been observed to occur with a median survival time of 9.2 months. However, HAART sometimes achieves far less than optimal results, in some circumstances being effective in less than 50% of patients due to medication intolerance/adverse effects, ineffective antiretroviral therapy and infection with a drug-resistant strain of HIV [6]. However, inadequate adherence to medication results in less or no benefit from HAART.

Reasons for non-adherence and non-persistence with HAART are varied and overlapping. Poor access to medical care, inadequate social support, and drug abuse contribute to non-adherence. The complexity of the HAART regimens, increased pill number, dosing frequency, meal restrictions, and side effects create intentional non-adherence also contribute to this problem [7].

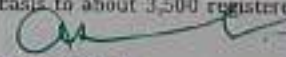
HIV prevalence in 2018 among adult population was estimated by National AIDS Control Organization (NACO), as 0.22%. In 2018, about 69,000 people died in India due to AIDS-related causes. The scale-up of free ART and rapid expansion of ART access since 2004 has saved cumulatively around 4.5 lakhs lives in India until 2014 [1-2].

However, in rural and semi-urban areas, HIV stigma is still prevailing. Many AIDS patients do not visit ART centers regularly and adhere to their regimens. Thus, the present study was initiated to assess the severity of infection, prescription regimens, adherence behavior among the AIDS patients registered at a district ART center.

METHODS

This observational, prospective, interview-based single-center study was approved by Institutional Human Ethical Committee and conducted for 6 months at Suryapet district ART center, Telangana. This center has about 8000 registered HIV-infected patients and this center dispenses ARV drugs free of cost, on monthly basis to about 3,500 registered




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RESEARCH ARTICLE

Formulation and Evaluation of Floating and Mucoadhesive Tablets containing Repaglinide

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ABSTRACT:

In the present study, Repaglinide an anti-diabetic drug is formulated in the form of floating mucoadhesive tablets to improve its bioavailability. Hydroxy Propyl Methyl Cellulose K200M, Sodium Carboxy Methyl Cellulose, Carbopol 974P, Karaya gum, Chitosan, Xanthan gum were used as rate controlling and mucoadhesive polymers in designing the tablets. Various formulations were prepared by using different concentration of polymers. The pre-compression blend of Repaglinide mucoadhesive tablets were characterized with respect to angle of repose, bulk density, tapped density, carr's index and hausner's ratio and all the results indicated that the blend had good flow property and better compressibility. The swelling studies were performed and the results indicated that all the formulations had good swelling index. The results of floating lag time and buoyancy studies suggested that formulations had good floating ability. The drug release studies indicated a controlled and enhanced drug release for a period of 12hrs. *In vivo* study was carried out using the optimized formulation. Based on the *in-vitro* drug release and other related evaluation tests, formulation RT11 containing drug: karaya gum in the ratio 1:2 was optimized. The drug release of the formulation RT11 followed Higuchi model with regression value of 0.984.

KEYWORDS: Repaglinide, Mucoadhesive tablets, floating, Mucoadhesive polymers.

INTRODUCTION:

The most acceptable route of drug administration to achieve a desired systemic action is oral route. There is a probability that at least 90% of all the drugs are administered through an oral route. In conventional oral drug delivery, the drug resides for a shorter period of time in the absorption window, so the bioavailability is hampered. Oral controlled drug delivery system represents the most popular form of controlled and prolonged drug delivery for the various advantages minimizing the cons of conventional therapy. This type of drug delivery systems releases the drug with constant or variable release rates¹⁻³.

Gastric emptying of a dosage forms can be modified by different parameters and can increase the gastric residence time of the dosage forms, by which the dosage form can remain in the stomach for a prolong period of time than the normal conventional dosage forms⁴. The most popular approach of oral controlled drug delivery is gastroretentive dosage form retain in stomach prolong period of drug profile and control the Gastric residence time in the stomach⁵. GRDDS can be elaborated as a modified technique of dosage form which can remain in the stomach for a long duration of time by altering the gastric emptying time as well as release the drug in a controlled manner, and then metabolized⁶. In the present scenario the different approaches for GRDDS have been designed to increase GRT. The primary objective of formulating GRDDS is to overcome the problems associated with existing oral conventional and sustained release dosage form and to design a drug delivery which will be more benefit towards the patients⁷⁻⁹.

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IMPACT OF PHARMACIST MEDIATED EDUCATION ON KNOWLEDGE, ATTITUDE, AND PRACTICES OF RURAL ADOLESCENT GIRLS TOWARD MENSTRUAL HYGIENE

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ABSTRACT

Objectives: The aim of the study was to study the influence of pharmacist-provided education on knowledge, attitude, and practices (KAP) of school-going adolescent girls toward menstrual hygiene practices in rural Suryapet, Telangana.

Methods: This study was a prospective interventional study. After obtaining the permission from the school, adolescent girls meeting the study criteria were included in the study. A 13-item KAP questionnaire was designed, validated, and administered to girls. A structured education was given about menstrual hygiene management to them. Post-education and the KAP questionnaire was readministered and results were analyzed.

Results: A total of 206 students were enrolled in the study and 90 (43.0%) students were in the age group of 14. Knowledge about menstruation was 27.18% in pre-test and it was 94.68% after post-test showing a significant ($p < 0.01$) improvement. After the education, the respondents have changed their opinion from "menstruation as a curse from God" (63.59%) to "as a natural process" (95.63%). Mother was named as the main information source about menstruation, followed by teachers and friends. Post-education increased the attitude of maintaining regular genital hygiene from 86.40% to 96.60%. Proper discard of menstrual waste to refuse bin increased from 54.85% to 95.15% indicating the overall improvement in knowledge, attitude, and practice regarding menstrual hygiene among adolescent girls.

Conclusion: Improvement in post-KAP scores suggests the positive impact of pharmacist mediated education on knowledge, attitudes, and practices among the rural school going girls.

Keywords: Menstrual hygiene, Menarche, Rural adolescent girls, Knowledge, attitude, practice.

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INTRODUCTION

Menarche is the onset of menstruation for the first time in an adolescent girl [1]. Earlier, it used to occur between 14 and 16 years. However, due to various reasons such as geographic variations, environmental conditions, and economic affordability of purchasing nutritious foods, the menarche age in young girls has reduced to 10–12 years [2]. Early menarche is called precocious puberty and has sociocultural, emotional, and health consequences. It can predispose to diseases such as cancers and heart disease [3].

Although menstruation is a normal vaginal bleeding that occurs due to uterus lining shedding, an important change occurs among girls during the adolescent years and continues till menopause [4]. It is always dealt with perceptions, secrecy among different cultures, and poor and inadequate sanitary facilities kept girls often away from attending schools. School-going girls from low-income families struggle to manage their monthly periods. They are constrained by practical, social, economic, and cultural factors. Most girls are ignorant about the physiology of menstruation and therefore the first experience of menstruation remains as fear, shame, and disgust [5]. Young girls find it difficult to manage menstrual hygiene in schools due to a lack of clean washrooms and privacy. Understanding and managing hygiene during menstruation is an essential feature for adolescent girls as it impacts health in terms of increased vulnerability to reproductive tract infections (RTI) and their complications such as chronic pelvic pain, dysmenorrhea, and in severe cases infertility due to poor hygiene practices [6].

As the cultural taboos and lack of awareness about menstrual hygiene management are prevailing among the rural folks, there is a need for improving awareness about menstrual hygiene. Thus, the present study

was designed to evaluate the effectiveness of the pharmacist-mediated educational intervention on school-going adolescent girls toward menstrual hygiene. Educational intervention includes assessment of the knowledge, attitude, and practices toward menstrual hygiene, promotion of safe and healthy menstrual practices, and prevention of reproductive tract infections.

METHODS

This was a prospective interventional study conducted in adolescent school-going girls in the age group of 12–16 years at selected upper primary schools in rural areas of Suryapet, Telangana over a period of 6 months. After obtaining the Ethical Committee approval and the necessary permissions from the school, adolescent girls fit into the inclusion criteria were enrolled in the study. Before initiating the education program, a 13-item validated questionnaire covering knowledge, attitude, and practice (KAP) regarding menstrual hygiene was prepared and validated. The KAP questionnaire was administered to the enrolled students. After collecting the pre-education KAP data, the students were given education regarding safe practices on menstrual hygiene and provided a printed information leaflet. After 4 weeks of education, the KAP questionnaire was readministered to observe the influence of education on knowledge, attitude, and practices toward menstrual hygiene. The collected KAP data (Pre and Post) were analyzed using the students' t-test where $p < 0.001$ is considered as statistically significant.

RESULTS

About 206 adolescent girls attending upper primary schools in nearby villages of Suryapet town were enrolled in the study. The average age for menarche in Telangana is reported as 12 years. The majority of respondent girls were in the age group of 14 years and studying



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Review Article

A SYSTEMIC REVIEW ON FLOATING MUCOADHESIVE DRUG DELIVERY SYSTEM

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Abstract:

Gastro retentive drug delivery system (GRDDS) is one of the novel approaches in the area of oral sustained release dosage form. Drugs that are easily absorbed from gastrointestinal tract (GIT) and have short half-lives are eliminated quickly from the systemic circulation require frequent dosing to achieve suitable therapeutic activity. The floating drug delivery systems increase the Gastric retention time providing wide therapeutic efficacy. Mucoadhesive drug delivery systems interact with the mucus layer covering the mucosal epithelial surface, and mucin molecules and increase the residence time of the dosage form at the site of absorption. The drugs which have local action or those which have maximum absorption in gastric pH require increased duration of stay in GIT. Thus, floating and mucoadhesive drug delivery systems are advantageous in increasing the bioavailability and enhanced therapeutic activity. In this regard, this review aims to provide information of different floating and mucoadhesive approaches and their importance.

Keywords: Bioadhesive, floating drug delivery, gastroretentive, mucoadhesive

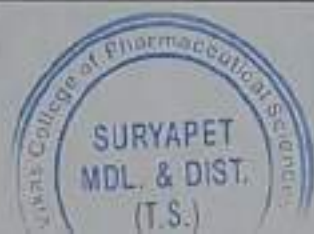
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PHARMACOEPIDEMOLOGICAL EVALUATION OF HIV PHARMACOTHERAPY AT DISTRICT ART CENTER IN SOUTH TELANGANA

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ABSTRACT

Objective: Objective of the study was to assess the drug utilization pattern of antiretroviral drugs, and medication adherence behavior among human immunodeficiency virus (HIV) patients attending a local ART center, Suryapet, South Telangana.

Methods: This was a prospective observational study approved by institutional ethics committee. Demographic, clinical, laboratory, and the treatment details were collected on daily basis for new cases and the data add on was collected for old cases. Medication adherence behavior was assessed through Morisky Medication Adherence Scale-8.

Results: During the study period, a total of 505 HIV patients were enrolled. Among them, majority patients were women (61%), in the age group of 31-45 (49.7%), illiterate (52.6%). Major mode of transmission identified was intimate contact (74%), and majority patients were in Stage I (49%). TLE regimen was prescribed in 69.9% patients and for children the prescribed regimen was ABC, 3TC, EFV (5.1%). About 43% patients were found with medium adherence.

Conclusion: This study concludes that the most prescribed regimens were combination of TLE, and majority of the patients were found with medium adherence.

Keywords: Antiretroviral therapy, Prescription pattern, Adherence behavior, Pharmacoepidemiological survey.

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INTRODUCTION

Pharmacoepidemiology is the study of use, effects and adverse drug reactions of medication in large number of populations with the purpose of supporting the rational and cost-effective use of medications in the population to improve the desired health outcomes [1]. The human immunodeficiency virus (HIV) is a retrovirus affects the immune system, destroying or impairing their function. As the infection progresses, the immune system becomes weaker, and the person becomes susceptible to infections [2]. Most advanced stage of HIV infection is called as acquired immunodeficiency syndrome (AIDS) and takes 10-15 years for an HIV-infected person to develop as AIDS case [3].

Use of HIGHLY ACTIVE ANTIRETROVIRAL THERAPY (HAART) substantially decreased death rate and translated AIDS as manageable condition. UNAIDS and WHO estimated AIDS death tolls as more than 25 million in 1981, when it was first recognized. [1] An adherence of 95% to ART is essential to achieve maximal viral suppression and minimize the opportunistic infections (OI) rate [4]. However, in clinical practice, maintenance of optimal ART adherence is challenging. A meta-analysis of 84 studies estimated that only 62% of HIV patients had achieved optimal adherence (of >90%) [5].

The present study aims at understanding prescribing patterns and medication adherence behavior of HIV patients visiting a district ART center. This helps in assessing the rational use of the antiretroviral drugs and strategies to reduce the infection rate and prolong the patient survival. Worldwide, more than twenty antiretroviral drugs belonging to Fusion inhibitors, NNRTI's, NRTI's, Chemokine receptor antagonist, Protease inhibitors, and Integrase inhibitors are licensed for focal therapy [6].

HAART is known as triple drug therapy. Studies have corroborated the combination therapy as very effective and reduce the viral load in the patients below detectable levels implying that HIV replication is

ceased [2]. In the absence of HAART, progression from HIV infection to AIDS has been observed to occur with a median survival time of 9.2 months. However, HAART sometimes achieves far less than optimal results, in some circumstances being effective in less than 50% of patients due to medication intolerance/adverse effects, ineffective antiretroviral therapy, and infection with a drug-resistant strain of HIV [6]. However, inadequate adherence to medication results in less or no benefit from HAART.


Reasons for non-adherence and non-persistence with HAART are varied and overlapping. Poor access to medical care, inadequate social support, and drug abuse contribute to non-adherence. The complexity of the HAART regimens, increased pill number, dosing frequency, usual restrictions, and side effects create intentional non-adherence also contribute to this problem [7].

HIV prevalence in 2018 among adult population was estimated by National AIDS Control Organization (NACO), as 0.22%. In 2018, about 69,000 people died in India due to AIDS-related causes. The scale-up of free ART and rapid expansion of ART access since 2004 has saved cumulatively around 4.5 lakhs lives in India until 2014 [1-2].

However, in rural and semi-urban areas, HIV stigma is still prevailing. Many AIDS patients do not visit ART centers regularly and adhere to their regimens. Thus, the present study was initiated to assess the severity of infection, prescription regimens, adherence behavior among the AIDS patients registered at a district ART center.

METHODS

This observational, prospective, interview-based single-center study was approved by Institutional Human Ethical Committee and conducted for 6 months at Suryapet district ART center, Telangana. This center has about 8,000 registered HIV-infected patients and this center dispenses ARV drugs free of cost, on monthly basis to about 3,500 registered


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MI RISK ASSESSMENT IN PATIENTS USING THE EZ-CVD RISK ASSESSMENT TOOL

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ABSTRACT

Objective: The objective of this study was to assess the myocardial infarction (MI) risk chances among individuals in the productive age group using easy cardiovascular disease (EZ-CVD) risk assessment tool.

Methods: This is a prospective observational and interventional study conducted for 6 months after obtaining the Institutional Human Ethics Committee approval. EZ-CVD risk assessment tool was used in this study which includes six self-reporting questionnaires such as age, gender, history of diabetes, history of smoking, history of hypertension, and family history of heart attack at the age of 60 or younger. A score of 6 or greater is considered as patients are at high risk of having MI.

Results: Sixty subjects were enrolled in to this study using the inclusion criteria. Among them, 36 were male and 24 individuals were female. Out of sixty recruited, 23 found having high risk for MI attack and 37 were at low risk of having chances of further MI.

Conclusion: The study conclude that EZ-CVD risk assessment tool was found useful to predict the occurrence of future MI.

Keywords: Myocardial infarction, Self-reporting questionnaire, EZ CVD risk assessment tool.

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INTRODUCTION

Cardiovascular disease (CVD) is one of the global health-related problems and became major cause for the mortality [1]. In 2016, about 17.8 million people died due to CVD and by 2030 it is expected to cause approximately 23 million deaths [2]. CVD refers to a class of clinical conditions such as coronary artery narrowing, stroke, heart failure, hypertensive heart disease, atherosclerosis, and myocardial infarction (MI). People in the age group of 50–65 are at high risk with continuous rise in low- and middle-income countries and slowly emerging MI as an epidemic problem [3,4]. Worldwide, mortality rate is estimated as 30% from 3 million people [4]. Every year, in US alone more than 370,000 deaths are occurring due to heart attack [5]. Where as in India, mortality is seen higher and is in over 10 million people. During the past 30 years, the disease rate has increased from 2% to 6% in rural population and 4% to 12% in urban population [6].

MI incidence rate was found significantly high among black men (75–84 years) compared to white among both men (9.1%) and women (7.0%) [7]. Risk of MI is seen 10.62% high in male smokers and 7.38% in non-smokers, whereas 5.88% in female smokers and 2.37% in non-smoker females. Studies conducted in 52 countries shown that men are more prone to high risk compared to women [8]. Age, gender, smoking, high blood pressure, hyperlipidemia, obesity, alcohol consumption family history of heart attack, sedentary life style, stress factors, and comorbidities such as diabetes, COPD, asthma, and chronic kidney disease are considered as risk factors for MI [9]. Globally, many tools are available to assess the risk of MI in the individuals with potential risk factors. One such tool is EZ-CVD tool [10], which is used to assess the risk qualitatively and gives an idea to prevent the MI risk through medical consultation and follow up. The EZ-CVD risk score is an easy-to-use risk score to predict cardiovascular events in adults utilizing only self-reported information without need for further laboratory or physical examination data. The risk score included six variables: Age, sex, a self-reported physician diagnosis of hypertension, diabetes mellitus, smoking, and family history of premature MI and had a similar predictive performance to the guideline-recommended ASCVD risk score. The EZ-CVD risk score could be easily used by physicians,

especially at primary care, to assess risk of patients and guide therapeutic decisions regarding statin therapy.

METHODS

This study was a prospective observational study, approved by the Institutional Ethics Committee, and conducted to assess the MI risk in individuals with various parameters, leading to precipitate heart attack. The data were collected for 6 months from January to June 2021. The patients who were attending to the cardiovascular and general medicine departments with potential risk factors were included in to the study to assess MI risk using Easy CVD (EZ-CVD) risk assessment tool and followed by counseling to avoid further complications and to minimize mortality rate and improve health-related quality of life among the patients.

Risk assessment tool

EZ-CVD risk assessment tool possess six questions (which include age, gender, history of diabetes, high blood pressure, smoking, and family history of heart attack at age 60 or younger) and evaluates the risk through self-reported scoring method. The risk is assessed based on the score points. If the score is six or more points, the patients are considered to have higher risk for future cardiovascular disease and should receive appropriate preventative therapy.

Data collection

Before conducting the study, the written informed consent was taken and the total study procedure was explained to the patients. Only the patients, agreed to give consent, were included in the study by taking their relevant information like demographic details, heart surgeries, mental status, obese, alcoholic, smoking, cardiac disease, and other activities which were collected in the patient data collection form by personal interview.

The enrolled patients were applied with EZ-CVD risk assessment tool that possesses six questions (which include age, gender, history of diabetes, high blood pressure, smoking, and family history of heart attack at age 60 or younger) to evaluate their risk through self-reported scoring

INDUCED STEVENS-JOHNSON SYNDROME IN A HUMAN IMMUNODEFICIENCY VIRUS PATIENT: A CASE REPORT

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ABSTRACT

Stevens-Johnson syndrome (SJS) is an acute life-threatening condition. In 95% of case reports, drugs were found to be an important cause for the development of SJS. About 100 drugs have been identified to causes of SJS. Very few reports were published on diclofenac-induced SJS. The incidence rate of SJS is approximately 1-2/1000 individuals with human immunodeficiency virus. In this case report, we present a 58-year-old female developed SJS after taking of diclofenac tablets.

Keywords: Stevens-Johnson syndrome, Diclofenac, Human immunodeficiency virus patients.

INTRODUCTION

Stevens-Johnson syndrome (SJS) is a rare but very serious disorder of skin and mucous membranes. It is usually a reaction due to a medication or due to an infection. Often, in SJS, patient experiences flu-like symptoms, followed by a painful red or purplish rash that spreads and blisters. This is later followed by the top layer of the affected skin to die and shed. It is considered as an acute life-threatening condition and a medical emergency and requires hospitalization. Eliminating the underlying cause, controlling the symptoms, and minimizing complications were the aim of the treatment. In SJS recovery takes weeks to months, depending on the severity of the patient's condition [1].

In 95% of the SJS cases, drugs are an identified as the important cause [2]. Infections or a combination of infections and drugs have also been reported as the etiology of the syndrome [3]. As per case reports and studies, more than 100 drugs have been identified as causes of SJS [4,5]. In human immunodeficiency virus (HIV) cases, the incidence rate of SJS was reckoned as 1-2/1000 HIV cases [6]. Although non-steroidal anti-inflammatory drugs (NSAIDs) are a rare cause of SJS in adults, these risks may not be ignored. The risk is much higher in older patients, women and immunocompromised patients [7].

CASE REPORT

A 58-year-old female patient came to our hospital with complaints of multiple rashes on skin all over the body, burning sensation in the oral cavity and lips. She is a known case of HIV acquired immune deficiency syndrome and on antiretroviral therapy since 3 years. On physical examination, lesions were observed on her lips, floor of the mouth, and the surface of the tongue. In addition, she had reddish lesions all over her all limbs as well as on the upper body. All of these manifestations supported the diagnosis of SJS (Fig. 1). History taking, clinical examination, serological test, and bacteriological culture tests were also conducted to rule out infectious causes of SJS.

The patient history suggests that she has used diclofenac tablets 50 mg for the last 2 weeks to treat her severe body pains took the medication as over-the-counter. It was her self-medication. Diclofenac tablets were discontinued and started with IV dexamethasone, oral levocetirizine, oral doxycycline, chloramphenicol eye drop, and betadine mouthwashes along with salbutamol nebulization for her breathlessness in the hospital. During the treatment period, the patient's lesions were

monitored closely after she got admitted to the hospital. After 5 days, lesions were started to disappear and after 2 weeks, she was healed with cutaneous and mucosal ulcers. The patient was recovered successfully and got discharged.


DISCUSSION

In 1922, Stevens and Johnson described 2 male patients of 7 and 8 years old, who developed extraordinary generalized eruption with fever and inflamed buccal mucosa [2,8]. Numerous studies have shown that adverse drug reaction related hospital admissions are up to 10% of the total number of hospital admissions [9].

SJS is frequently associated with drug use. More than 100 drugs have been associated with the development of SJS that is reported as a single case report or retrospective studies. Three most classes of drugs responsible for SJS are antimicrobials, NSAIDs, and anti-epileptic drugs. Causing SJS in descending order of frequency are cephalosporins, quinolones, aminopenicillins, tetracyclines, macrolides, imidazole antifungals, and anticonvulsants (phenobarbital, phenytoin, valproic acid, carbamazepine, and lamotrigine), and then NSAIDs (especially piroxicam), allopurinol, and others are known to cause SJS. Among NSAIDs, paracetamol was found the most common cause of skin reaction in Indian studies [2,10]. Furthermore, valproic acid, NSAIDs, and acetaminophen were significantly associated with SJS in children [11]. SJS is a severe adverse drug reaction characterized by widespread lesions affecting the eyes, mouth, larynx, pharynx, esophagus, skin, and genitals. It almost involves oral mucosa [7,12].

For overlapping SJS (when 15-30% body surface area involvement exists), oxican class of NSAIDs such as piroxicam, meloxicam, tenoxicam, and sulfonamide are most commonly implicated to cause SJS in the United States and other western nations. In contrast, allopurinol has been reported as the most common offending agent in the Southeast Asian nation [13].

In this case, diclofenac sodium was found to be as cause for SJS based the patient's recent medication consumption history. The causality assessment of diclofenac-induced SJS, in this case, was done. The scores on WHO probability scale and Naranjo's suggest that the event was possible. To resolve the SJS symptoms, patient will be recommended with topical silver nitrate 0.5% or chlorhexidine 0.05% along with oral antibiotics to treat skin lesions and to prevent secondary infections [7]. In this patient, oral doxycycline, betadine mouthwash and


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A Study of medication administration errors in a tertiary care hospital

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ABSTRACT

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Medication administration errors account for 34% of all medication errors and identified as one of the important reasons for patients' morbidity and mortality. NPSA statistics show that 59.3% of medication errors occur during the administration stage. Thus identifying and resolving the administration errors will improve the patient care and decreases the health care costs. National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) taxonomy was used to analyse the frequency, types, severity and factors responsible for medication administration errors. The findings of the study reveal that the frequency of medication administration errors is 15.34%, omission errors (33.02%), improper dose (17.43%) and wrong time (12.84%) errors were the major types of errors occurred and the majority administration errors belonged to category C (112), B (46) and D (35). Frequent interruptions and distractions, lack of communication between health care professionals, performance deficit and work stress on duty nurses are identified as major factors responsible for administration errors.

Keywords: Medication Administration Errors (MAEs), National Coordinating Council for Medication Error Reporting (NCC MERP) taxonomy, National Patient Safety Agency (NPSA) and Patient Care.

INTRODUCTION

Medication use in hospitals is a complex process and depends on successful interaction among health care professionals functioning at different areas. Medication errors may occur at any stage of prescribing, documenting, dispensing, preparation, or administration.¹ Medication errors may contribute to morbidity, mortality and increased health care costs.² In 2007, National Patient Safety Agency (NPSA) statistics shows that 59.3% of medication errors occur during the administration stage.³ Medication administration errors are defined as any deviation from the physician's medication order as written on patient's treatment chart during medication administration to patient.² The plan for administering a medication begins with identifying the patient, the drug, the dose, the route, and the time.⁴ In 1995, the National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) classified administration errors in to wrong drug, wrong route, wrong dose, wrong patient, wrong timing of drug administration, contra-indicated drug, wrong site, wrong dosage form, wrong infusion rate and expired medication. Such errors may occur intentionally or

unintentionally.² The elderly, and mentally ill patients are particularly more susceptible as they may be confused, resist medication administration, physically weak and require complex medication regimens.⁵ In a study conducted over a period of three and half years in UK at a psychiatric hospital, the most frequent types of errors observed were the improper dose, wrong drug, and dose omission.⁶ The drugs often associated with harmful events of medication errors in pediatric patients include morphine, insulin, vancomycin, potassium chloride, gentamicin, ceftriaxone, and heparin.⁷

In addition to the morbidity and mortality, medication errors also contribute to increased health care costs. The department of health in UK, estimated the direct and indirect health care expenditure due to medication errors as 2£ billion.⁴ In US, an American health care system estimated the medication errors related expenditure as \$37 billion per year.⁸

Medication administration has become more complex as a result of the increasing number of medications available and new routes of administration. Nurse is considered as vital in medication administration process and the literature review states that poor calculation competency of nurses, poor adherence to protocols and poor knowledge of medications are the important reasons leading to medication administration errors.⁴

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