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ORIGINAL ARTICLE / ÖZGÜN MAKALE



MOLECULAR DOCKING STRATEGY FOR MULTI-TARGET INHIBITOR DISCOVERY OF SELECTED PLANT CONSTITUENTS IN BAUHINIA ACUMINATA

BAUHINIA ACUMINATA'DAKİ SEÇİLMİŞ FİTO BİLEŞENLERİN ÇOK HEDEFLİ İNHİBİTÖR KEŞFİ İÇİN MOLEKÜLER YERLEŞTİRME STRATEJİSİ

Muni Sireesha SUNKARA¹, Vinutha KUCHANA¹, Neelima KUDUMULA^{1*}

¹Osmania University, Sarojini Naidu Vanita Pharmacy Mahavidyalaya, Department of Pharmaceutical Chemistry, 500017, Hyderabad, India

ABSTRACT

Objective: Traditional medicine is often considered to be a kind of complementary or alternative medicine (CAM) nowadays. Therefore, documenting and identifying the herbs that are effective in treating various diseases is vital for future disease control programs. This study aims to perform a molecular docking analysis of the thirteen plant components in Bauhinia acuminata against the target proteins in lung cancer (PDB IDs: 2ITY), breast cancer (1A52), diabetes (3L4U), obesity (IT02), inflammation (5COX) and corona viral infections (6VYO).

Material and Method: All the plant components used for the present study were retrieved from the plant Bauhinia acuminata and were evaluated for their biological activity results using molinspiration. Further insilico docking analysis was performed using AutoDock Vina software and the binding interactions were visualized using Discovery studio program.

Result and Discussion: The docking scores and analysis of the interactions of the plant components with targets suggest that all the selected plant components showed excellent binding to the chosen targets when compared to that of the standard drugs. As a result of the docking process on 6 different targets, the selected plant components like Quercetin, Beta-sitosterol, and Rheagenine were observed to show good binding energy values against all the 5 targets except 6VYO as shown in (Table 9). These results can further pave the way for getting better insights in identifying and designing potential lead candidates.

Keywords: AutoDock Vina, Bauhinia acuminata, discovery studio, molecular docking, plant components

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e-mail / e-posta: neelima kudumula@yahoo.com, Phone / Tel.: +919502792574

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^{*} Corresponding Author / Sorumlu Yazar: Neelima Kudumula

Research Article



Multi-Targetted Molecular Docking Analysis of Selected Phytoconstituents of Bauhinia acuminata

S. Muni Sireesha, K. Neelima, K. Vinutha*

Department of Pharmaceutical Chemistry, Sarojini Naidu Vanita Pharmacy Maha Vidyalaya, Osmania University, Hyderabad, India. *Corresponding author's E-mail: vinutha_me@yahoo.co.in

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ABSTRACT

Traditional medicine is often considered to be a kind of complementary or alternative medicine (CAM) nowadays. Therefore, documenting and identifying the herbs that are effective in treating various diseases is vital for future disease control programs. The study aims to perform Molecular docking analysis of the phytoconstituents of the Bauhinia acuminata named Quercetin, Bauhinone, Beta-sitosterol, and Kaempferol 3-glycoside with the target proteins with PDB IDs namely 2ITY, 1A52, 3L4U, IT02, 5COX, 6VYO involved in Lung cancer, breast cancer, anti-diabetes, anti-obesity, anti-inflammatory, and SARS COV-2. Chemsketch software, the study of the in-silico docking was done using Autodock.4.2 software and the binding interactions are visualized using Discovery studio 3.1. The docking scores and analysis of the interactions of the phytoconstituents with target proteins suggests that all the selected 5 phytoconstituents showed excellent binding to 2ITY and 5-COX as opposed to the standard drugs Erlotinib and Aspirin. In this study, it was concluded that the investigated phytoconstituents showed potent inhibiting activity, and the dock scores as opposed to standard as in Table 6, directly represent possible binding to the target proteins indicating their good biological activity as in lung cancer and anti-inflammatory action.

Keywords: Autodock 4.2, Bauhinia acuminata, Discovery studio 3.1, Molecular docking, Phytoconstituents.

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INTRODUCTION

raditional medicine defines by the World Health Organization (WHO) as: "the summation of total knowledge, practices, and skills based on the historical theories, beliefs, and experiences to maintain the human or animal health and to prevent, diagnose, improve, or treat physical/mental illnesses" in indigenous to various cultures ¹.

Herbal remedies are widely used in both developing and developed world countries to treat various illnesses indispensable ². The WHO reported, to treat their illnesses about 80% of the world's population are depending primarily on traditional medicines. Traditional medicine is often considered a kind of complementary or alternative medicine (CAM) ³ nowadays. Herbal medicines include herbal preparations, raw herbs, and finished herbal products, as well as additives derived from different kinds of plant parts/herbs. Many advantages are shown by the active components of these herbs, like lower toxicity and allergenicity than when compared to some commercial medications, regulating immunological responses, and causing viral destruction ⁴. In the research trials ⁵, to prevent viral infections various common herbs have been

utilized, and their effectiveness has been established. Therefore, documenting and identifying the herbs that are effective in treating various contagious diseases is vital for future disease control programs.

Bauhinia acuminata is an evergreen shrub belonging to the family of Fabaceae grown in the areas of Southeast Asia such as Malaysia, Indonesia, or the Philippines. For conventional drugs, bark, leaves, stem, blooms, and roots have been utilized. In India, it is a traditional plant, and its extract in studies have shown that Bauhinia acuminata have significant biological activities such as in the treatment of lung cancer ⁶, breast cancer ⁷, anti-diabetic ⁸, anti-obesity ⁹, anti-inflammatory ¹⁰. Based on the reported anti-lung cancer, anti-breast, anti-diabetic, anti-obesity activities, molecular docking studies have been planned to establish the contribution of the activity by the phytoconstituents.

Bauhinia acuminata has been chemically studied and reported wherein the important chemical constituents isolated from Bauhinia acuminata are around 13 but 4 among them are chosen for our studies such as Quercetin, Bauhinione, Beta-sitosterol, and Kaempferol-3-glycoside. Therefore, these 4 phytoconstituents will be evaluated in this study on the docking behavior of EGFR ¹¹, ESTROGEN ALPHA RECEPTOR ¹², ALPHA GLUCOSIDASE ¹³, HMG COA ¹⁴, 5COX ¹⁵, SAR COV-2¹⁶ using an Insilco molecular docking analysis with Autodock.4.2 software and also an investigation on the enzymes binding sites using Discovery Studio Version 3.1.



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A REVIEW ON HERBAL DRUGS WITH POTENTIAL ANTI-ARTHRITIC ACTIVITY

Shanaz Banu ¹ and Leemol Varghese *2,3

Department of Pharmacognosy ¹, Dayananda Sagar University ², Bengaluru - 560078, Karnataka, India. Sarojini Naidu Vanita Pharmacy College ³, Hyderabad - 500017, Telangana, India.

Keywords:

Rheumatoid arthritis, Phytoconstituents, Early Diagnosis, Drug treatment

Correspondence to Author: Mr. Leemol Varghese

Assistant Professor, Sarojini Naidu Vanita Pharmacy College, Hyderabad - 500017, Telangana, India.

E-mail: leemolvarghese1@gmail.com

ABSTRACT: Rheumatoid arthritis (RA) is a general inflammatory disorder touching about 1.3% of the grown-up census of the world. Over the last two decades, a significant development has been done in the thoughtfulness of RA pathophysiology, best outcomes, and successful treatment strategy, and the credit of the significance of diagnostic agents and treating RA near the beginning. Earlier than novel treatments were obtained, RA caused notable incapability and deaths. At present, it is customary that principal diagnostic agents and therapy are significant and helpful. Development in the treatment of RA made it likely to manipulate signs in inflammatory arthritis. The early hour diagnosis and treatment of RA can prevent or reduce the progression of joint erosion to about 90% of patients; by this means irreversible disability can be prevented. In advance and more effective treatment significantly improves the prognosis of RA. The advancement of novel instruments to assess disease activity and recognize remission has brought about innovative treatment strategies to inhibit RA ahead of joint damage forever. The pharmacological therapy consists of the nonsteroidal anti-inflammatory drug (NSAIDs), glucocorticoids (GC); disease-modifying antirheumatic drugs (DMARDs), biological drugs is of two types: 1) Monoclonal antibodies, 2) bisphosphonate agents. The price of a few treatments is considerable, but their use has come down with the advancement of biosimilars. A target-treatment strategy aims to decrease disease activity by around 50% in three months and achieve a reduction of disease succession in six months, with continuous therapy if needed, which can prevent RA-related disability. There is a restoration of attention in plant products because of the present belief that green medicine is safer and more trustworthy than expensive synthetic drugs. The outlook is towards the synchronized multidimensional research intended to correlate botanical and phytochemical activities to exact anti-arthritic activity is achieved.

INTRODUCTION: RA is an inflammatory rheumatic disorder in which moving articular and extra-articular parts cause ache, disability, and death ^{1, 4}. It causes chronic inflammation, which is a systemic autoimmune disorder, at first disturbing to small bones and then the larger ones, eventually to skin, eyes, heart, kidneys, and lungs.



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Frequently, joints and cartilage of bones are damaged; tendons and ligaments are destroyed ^{5, 7}. Constant inflammation causes erosion of joints and practical injury in the huge bulk of patients ^{8, 11}.

RA results in severe ache, bulge, rigidity, and lack of activity in bones. It damages any bone still commonly affects bones of the wrist and fingers. Further, women are affected than men by RA. It usually begins in middle age and is very general in elderly people ^{12, 15}. Natural products from plants play an extraordinary function in treating and prevent many pathological conditions from olden times. Research examined by World Health Organization (WHO) has concluded that

In silico Molecular Properties Predictions of Novel Camalexin Derivatives

K.Mounika¹, J.Sumedha², G.Raveena³, K.Shivani⁴, K.Neelima⁵, S.Muni Shireesha⁶, Sandala Anuradha Bai^{7*}

^{1,2,3,4,5,6,7}Department of Pharmaceutical Chemistry, Sarojini Naidu Vanita Pharmacy Maha Vidyalaya, Tarnaka, Hyderabad.500007, Telangana, India

*Corresponding Author Email: anusandala@gmail.com

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ABSTRACT

A novel method presentsinitial, assessment of efficacy and biopharmaceutical Properties of drug candidates. Information concerning pharmacokinetics, toxicity would be helpful for creating an effective drug, so in primaryphase of development ADMET properties are to be considered. CADD is used for optimization of properties by maintaining affinity. It is used to identify the lead molecule by virtual screening. Camalexin, an indole phytoalexin is derived from Arabidopsis thaliana (Cruciferaceae) that exhibits antibacterial, antifungal, anti-tumor effects against leukemia and prostate cancer by inducing apoptosis. Present study to design novel Camalexin Derivatives, analyse the Physicochemical and Pharmacokinetic parameters through the online software's SwissADME, and Molinspiration. We designed 19 novel camalexin derivatives and predicted their molecular properties which are important for drug candidate. The results exhibit that, compounds stratify to Lipinski's, so they should theoretically manifest good oral absorption. This acceptability with respect to Lipinski rule proves them as safe administrable drugs and establishes their pharmacological activity.

INTRODUCTION

A novelplan in drug discovery came on the track, for initialassessment of potency, choosiness of lead molecules, and their potential ADME/Tox tasks. This aids to decrease cost, late-stage failures and accelerate fruitful development of new molecular entities. Computer-aided drug design (CADD) is a widely used term that signifies computational tools, resources for the storage, management, analysis and modelling, of compounds (*Bernardo P.H,et al.*,2009). CAD enables the development, modification and optimization of design process

An in Silico model for predicting oral bioavailability can be achieved with an appropriate balance between solubility and partitioning properties (Cushman DW et al., 1977). The molecular properties of compounds can be calculated using Mol inspiration, Drug like is defined as those compounds that have sufficiently acceptable ADME properties and sufficiently acceptable toxicity properties to survive through the completion of human phase 1 clinical trials.

Indole phytoalexins have been shown to exhibit significant anti-cancer, chemo preventive, and antiproliferative activity. Camalexin is the characteristic phytoalexin which isisolated from *camelina sativa* and *Arabidopsis* [cruciferae] with antibacterial, antifungal, antiproliferative and anticancer activities and can induce reactive oxygen species [ROS] production. Camalexin is an indole phytoalexin is indole substituted at position 3 by a 1,3-thiazol-2-yl group and a member of 1,3- thiazoles. It has a role as a metabolite. (*William A.Ayer, et al.*, 1992).

Benzyl camalexin, Indole alkaloid camalexin. The anticancer activity of camalexin is due to substitutions like3,4,5-trimethoxypropyl,3,4-dimethoxyphenyl,4-benzyloxy-3-methoxyphenyl,4-piperidinyl,4-fluorophenyl and N-methylindole are helpful for anticancer activity/.In cancer cells the benzocamalexin (BC) displayed the most potent activity with an IC50 value of 23.3–30.1 μmol/L. On the other hand, negligeable toxicity (IC50 > 100.0 μmol/L) in non-cancer cells was observed. The results expressed that BC was selected for further studies. The benzocamalexin (BC) displayed the most potent activity with an IC50 value of 23.3–30.1 lmol/L. On the other hand, minimal toxicity (IC50 > 100.0 lmol/L) in non-cancer cells. BC-induced arrest of the cell cycle in the G2 phase associated with downregulation of a-tubulin, a1-tubulin, b5-tubulin expression. The inhibitory effect of BC is mediated via inhibition of microtubule formation, the obstruction of cell cycle development and start of apoptosis may play an significant role in the antiproliferative activity of BC in human



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INVITRO PANCREATIC LIPASE, ALPHA AMYLASE, ALPHA GLUCOSIDASE INHIBITORY ACTIVITY OF BERGAPTEN

V. Jyothi*, Leemol S., Rajeshwari M., Muni Sirisha S. and P. Praneetha

Department of Pharmacognosy Sarojini Naidu Vanita Pharmacy Maha Vidyalaya, Vijayapuri Colony, Tarnaka, Secunderabad. Telangana State.

*Corresponding Author: Dr. V. Jyothi

Department of Pharmacognosy Sarojini Naidu Vanita Pharmacy Maha Vidyalaya, Vijayapuri Colony, Tarnaka, Secunderabad. Telangana State.

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ABSTRACT

In the present study the furanocoumarin, Bergapten was studied for in-vitro alpha (α)-amylase, alpha (α)-glucosidase and pancreatic lipase inhibitory activities. The aim of this work is to evaluate the inhibitory activities of the phytochemical Bergapten at different concentrations. Diabetes mellitus is a clinical condition characterized by hyperglycemia in which an elevated amount of glucose circulates in the blood plasma. Alpha amylase and alpha glucosidase inhibitors are used to achieve greater control over hyperglycemia in type 2 diabetes mellitus. The present study intends to screen novel pancreatic lipase, alpha amylase and alpha glucosidase inhibitors from natural sources like plants in order to minimize the toxicity and side effects of the inhibitors currently used to control obesity and hyperglycemia. The phytochemical Bergapten exhibited significant α -amylase, α -glucosidase and pancreatic lipase inhibitory activities with an IC50 value $8.54\mu g/ml$, $9.11\mu g/ml$ and $7.22\mu g/ml$ respectively and well compared with standard acarbose for alpha (α)-amylase and alpha (α)-glucosidase and or listat for pancreatic lipase inhibitory activities respectively.

KEYWORDS: Bergapten, alpha amylase, alpha glucosidase, pancreatic lipase.

INTRODUCTION

Obesity is a major visible global problem and yet most neglected public health issue. It is a condition where a person has accumulated abnormal or excess body fat that causes risk to health. It is an imbalance between energy intake and expenditure.

World health Organization defines over weight and obesity as abnormal or excessive fay accumulation. It possesses a major risk for serious diet related non-communicable diseases such as coronary heart disease, hypertension, stroke, non-insulin dependent diabetes mellitus, gall bladder disease, dyslipidemia, osteoarthritis and gout and pulmonary disease.

The treatment involves dietary management, Physical activity, exercise, anti-obesity drugs and gastric intestinal surgery. The anti-obesity drugs interfere with the normal body fundamental process and lead to side effects. The anti-obesity drugs have serious adverse reactions. Hence due to high cost and potential serious side effects the natural products are an alternative method to treat obesity. The antihyperlipidemic activity is shown by the plants mainly belonging to the families Leguminosae, Laminaceae, Liliaceae, Rosaceae, Moraceae, Asteraceae, Cucurbitaceae and Araliaceae. [1.2,3]

Diabetes is a chronic disease and a serious metabolic disorder characterised by hyperglycaemia or raised blood sugar. The person is incapable to either produce or utilize insulin. According to statistics 2.8% of the world's population suffer from this disease and it is expected to increase to 5.4% by 2025.^[4]

The treatments for control of diabetes include insulin therapy, pharmacotherapy, and diet therapy. are available to control diabetes. The mechanisms include stimulation of insulin secretion, increase of peripheral absorption of glucose, delay in the absorption of carbohydrates from the intestine and reduction of hepatic gluconeogenesis etc.^[5,6,7]

The side effects associated with synthetic anti-diabetic drugs include skin problems, weight gain, risk of liver disease, anaemia, hypoglycaemia, abdominal gas, fluid retention, ankle swelling etc.^[8] Hence anti diabetic drugs from medicinal plants have been developed which are found to be having lesser side effects.

Human pancreatic lipase is the main enzyme that breaks down dietary fats in the human digestive system. Pancreatic lipase hydrolyzes from triglycerides into glycerol esters, 2-monoacylglycerols, glycerol, and free fatty acids mainly in the intestine. Pancreatic α -amylase

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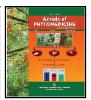
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In silico studies in the prediction of novel isoxazole derivatives as potentially active anticancer agents

Munisireesha Sunkara, Hemalatha Sattu*, Pranitha Balasani, Neha Patil and Ambika Belakara

Department of Pharmaceutical Chemistry, Sarojini Naidu Vanita Pharmacy Maha Vidyalaya, Tarnaka, Hyderabad-500017, Telangana, India

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Molinspiration

Abstract

Isoxazoles have engaged a distinctive position in heterocyclic chemistry and their derivatives have significant pharmacological effects. The active pharmacophores of various isoxazole analogs are accountable for antifungal, anticancer, antiviral, antidiabetic, analgesic, antitubercular, anti-inflammatory and other activities. In this research, all the designed compounds were subjected to various pharmacokinetic and pharmacodynamic properties by using in silico tools. Isoxazole derivatives were designed and their molecular properties and toxicity prediction studies were carried out to know the safety and efficacy by using molinspiration, molsoft and swissADME. Top lead molecules were identified and subjected to molecular docking. Docking studies were accomplished to find the probable protein-ligand interactions. The thirty designed compounds were docked against the target protein (Pdb ID: 3QAQ). Approximately, hundred diverse protein-ligand complex conformations for every docked complex were produced through MGL tools, the Autodock suite. Among the docked ligands, compounds 5,7,10,13,15,17 and 24 conveyed the lowest binding energy between - 9.5 to - 8.8 kcal/mol. The binding energy of all the compounds reached from - 7.1 to - 9.5 kcal/mol. The compounds 7,10,13 and 24 possess the same hydrogen bonds, each with ARG:849, ARG:690, amino acids are standard regorafenib. Finally, the docking results conclude that compounds 7 (- 9.5 kcal/mol) 10 (- 9 kcal/mol), and 17 (- 9 kcal/mol) possess two hydrogen bonds with the best binding energy values. Subsequently, an ADMET study was done for ligand appropriateness as a drug candidate. Thirty docked compounds were assessed for their biological properties and compared with the standard drug regorafenib.

1. Introduction

Heterocyclic compounds have captivated observable attention as they elucidate the relationship between chemical and life sciences (Kapubalu *et al.*, 2011). Heterocycles that hold atoms like oxygen and nitrogen are recognized as a predominant class in medicinal chemistry. Isoxazole is a five-membered heterocyclic compound with O and N (Sagar *et al.*, 2017).



The isoxazole ring was first synthesized by Dunstan and Dymand. The chemistry of isoxazole is developed in between 1930-1946. The study is contributed from Quilico's studies from nitrile oxides and un-saturated compounds. The common name for 5-membered unsaturated heterocycles as isoxazole was primitively put forwaded by Hantszch (Kuntal Manna *et al.*, 2014). In the past decades,

Corresponding author: Dr. S. Hemalatha

Professor, Department of Pharmaceutical Chemistry, Sarojini Naidu Vanita Pharmacy Maha Vidyalaya, Tarnaka, Hyderabad-500017, Telangana, India

E-mail: hemalathasattu0@gmail.com

Tel.: +91-7075921012

Copyright © 2022 Ukaaz Publications. All rights reserved. Email: ukaaz@yahoo.com; Website: www.ukaazpublications.com remarkable efforts were made to synthesize isoxazoles due to their properties (Nagajyothi et al., 2015). 1,3 dipolar cyclo-addition of alkenes and alkynes is the major method used for synthesis of isoxazole ring (Soumyadip Das et al., 2021). Isoxazoles are widely explored in therapeutics such as antibacterial, antitumour, antitubercular, anticancer, ulcerogenics, antileishmania, etc. (Sagar et al., 2017). Isoxazole ring is present in some of thetherapeutic drugs, including lactam antibiotics-cloxacillin, dicloxacillin, antibacterials-sulfamethoxazole, COX-Ï inhibitor-valdecoxib, DMARD (immmuno supressive disease modifying antirheumatic drug) leflunomide (Afzal Shaik et al., 2019). Isoxazoles have some industrial efficiency, reduced isoxazole derivatives such as antibioticcycloserine and MAO inhibitor-isocarboxazidis useful in psychotherapy and denazolanis a isoxazole steroid that exhibits anabolic activity. Isoxazole is best described as a resonance hybrid of many resonance structures. The heteroatoms present in the ring impact the rate of electrophilic substitution in the ring. It is unstable towards nucleophilic agents action that causes the cleavage of isoxazole ring that yields beta-keto nitriles as the end products (Leach et al., 2006). Isoxazole is also used in material science, such as photochromic, electrochemical probe for Cu⁺² and also has optical properties in dye-sensitized solar cells, liquid crystal. Some of the marketed drugs with isoxazole nucleus are oxacillin, cycloserine, acivicin, broxaterol, isoxaflutole, sulfame-thoxazole, etc.

Review Article



A Review on Psoriasis: Treatable, but not Curable

Balusu Haarika*1, Garvandha RamyaRani2, Devarakonda Sunidhi2, Thavidaboina Sowmya2

*¹Department of pharmaceutics, Sarojini Naidu Vanita Pharmacy Maha Vidyalaya, 12-5-31/32, Vijayapuri colony, Tarnaka, Secunderabad, 500017, Telangana, India.

²Department of Pharm. D, Sarojini Naidu Vanita Pharmacy Maha Vidyalaya, 12-5-31/32, Vijayapuri colony, Tarnaka, Secunderabad, 500017, Telangana, India.

*Corresponding author's E-mail: Haarikabalusu09@gmail.com

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ABSTRACT

Psoriasis is a chronic proliferative inflammatory skin disorder. Erythematous plaques with silvery scales are covered in Extensor surfaces, scalp, and lumbosacral area, The disease can also impair the eyes and joints. It is one of the most prevalent dermatological diseases and a continuous challenge in regards to therapeutic approach. The appearance of psoriasis is described by the Koebner Phenomenon. There are two types of psoriasis, Type 1 psoriasis has a positive family history, begins before the age of 40, and is linked to HLA-Cw6; Type 2 psoriasis has no family history, begins after the age of 40, and is not linked to HLA-Cw6. The Body Surface Area (BSA), Physician's Global Assessment (PGA), Psoriasis Area and Severity Score (PASI), and Dermatology Life Quality Index are the most often used measures for assessing plaque psoriasis severity (DLQI), Psoriasis Area Severity Index (PASI) is the most extensively used assessment instrument for determining the severity of the illness and evaluating the treatment effectiveness. Topical treatment is employed for mild to moderate Psoriasis; biologics have a pragmatic strength of recommendation, which is often based on the patient's case evidence and the drug's performance. According to the American Academy of Dermatology and the National Psoriasis Foundation, biologic drugs are "engineered monoclonal antibodies and fusion proteins that exert their therapeutic activities by inhibiting cytokine receptors crucial to psoriatic inflammation".

Keywords: Psoriasis, chronic skin disease, Biologic's, Inflammation, Engineered monoclonal antibodies.

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INTRODUCTION

soriasis is a skin disorder that is chronic proliferative and inflammatory in nature. Extensor surfaces, scalp, and lumbosacral area are covered in erythematous plaques with silvery scales. The disease can also impair the eyes and joints. It has no cure. Because of their low quality of life, many psoriasis patients experience depression^{1,2,3}. In addition to the cutaneous manifestations, it is associated with an increased risk of psoriatic arthritis, depression and cardiovascular disease. ¹²

Psoriasis has various varieties, but the plaque form is the most prevalent, affecting the trunk, extremities, and scalp, White silvery scales are seen when plaques are examined closely. The eye is implicated in roughly ten percent of cases. 1,2,3

The global prevalence is estimated to be around 2%, Asian and some African ethnicities have lower rates, whereas Caucasian and Scandinavian populations have a higher rate of 11%. The epidermal thickening is caused by aberrant

interactions between T cells, immune cells, and inflammatory cytokines. Due to racial considerations, genetic background, lifestyle, and other variables, the prevalence rate varies byarea⁹.

It is one of the most prevalent dermatological diseases and a continuous challenge in regards to therapeutic approach¹⁰.

Etiology

The specific cause is uncertain; however, it is a T lymphocyte-mediated autoimmune illness. Many psoriatic patients, primarily from distinct racial and ethnic groups, show an association of HLA antigens, its presence in families shows a hereditary susceptibility. Psoriasis lesions are caused by mechanical, chemical, and radiational damage⁴.

Chloroquine, lithium, beta-blockers, steroids, and nonsteroidal anti-inflammatory medications (NSAIDs) can aggravate psoriasis, Psoriasis improves in the summer, whereas it worsens in the winter. Other triggering factors for psoriasis include infections, psychological stress, alcohol, smoking, obesity, and hypocalcaemia⁴. Psoriasis with pustules appears to be genetically different, with varying degrees of vulnerability¹⁶.

The illness has a complex genetic foundation, with 60-80% of white psoriasis patients carrying HLA-Cw6 compared to 20% of the population of the same breed. Psoriasis



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PHARMACEUTICAL SCIENCES AND RESEARCH



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DESIGN AND *IN-VITRO* CHARACTERIZATION OF CHLORDIAZEPOXIDE EFFERVESCENT FLOATING TABLETS

Haarika Balusu *, Tanvi Mathur, Yeredla Swathi, Amenah Haitham Mezher Aljubori and Sravya Maddukuri

Department of Pharmaceutics, S. N. Vanitha Pharmacy Maha Vidyalaya, 12-5-31/32, Vijayapuri Colony, Tarnaka, Secunderabad - 500017, Telangana, India.

Keywords:

Chlordiazepoxide, Effervescent floating tablets, Methocel K₄M, Methocel K15M & Xanthan gum

Correspondence to Author: Dr. B. Haarika

Professor and HOD, Department of Pharmaceutics, S. N. Vanitha Pharmacy Maha Vidyalaya, 12-5-31/32, Vijayapuri Colony, Tarnaka, Secunderabad - 500017, Telangana, India.

E-mail: haarikabalusu09@gmail.com

ABSTRACT: Chlordiazepoxide is a sedative and hypnotic medication which is used to treat anxiety, insomnia, and withdrawal symptoms from alcohol and/or drug abuse. Chlordiazepoxide has a medium to the long half-life, but its metabolite is pharmacologically active and has a very long half-life. In the present work, an attempt has been made to develop effervescent floating tablets of Chlordiazepoxide. Methocel K4M, Methocel K15M & Xanthan gum were employed as polymers. All the formulations were prepared by direct compression method using 6mm flat punches. The blend of all the formulations showed a better angle of repose, bulk density, tapped density, compressibility index, and Hausner's ratio. The prepared tablets exhibited excellent hardness, friability, drug content, buoyancy lag time, duration of buoyancy, swelling index. Among all the formulations, the F7 formulation floated for more than 12 h, showed short buoyancy lag time of 96±0.92 seconds, high swelling indices of 2.4±0.12 %, and showed maximum cumulative percent drug release of 98.21±0.24 % in 12 h. Consequently, formulation F7, made using xanthan gum in 10mg/unit tablet weight concentration, was considered as an optimized formulation. The mechanism of drug release was found to be following zeroorder release kinetics and non-Fickian diffusion.

INTRODUCTION: Chlordiazepoxide, a benzo-diazepine derivative, is mainly employed to treat anxiety and acute alcohol withdrawal symptoms and fear before surgery ¹. Floating drug delivery systems offer gastric retentive behavior, improved drug absorption, increased gastric residence time and make the formulation spend more time at its absorption site, controlled delivery of drugs, delivered drugs for local action, and minimized mucosal irritation due to the drugs, and site-specific delivery ².



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Chlordiazepoxide is a benzodiazepine BCS class II drug that binds to the GABA receptor and aggravates the inhibitory neuronal activity of GABA receptor ³. Oral Chlordiazepoxide is rapidly and completely absorbed; peak plasma concentrations appear 30 min after dosing. Chlordiazepoxide is mostly absorbed from the upper gastrointestinal tract and stomach ⁴.

Multiple-dose treatment leads to the accumulation of parent drugs and active metabolites, which precedes extreme sedation, respiratory depression, and muscle fatigue. Chlordiazepoxide conventional dosage form has more dosing frequency, which causes plasma peak fluctuation. Therefore, Chlordiazepoxide given through the gastro retentive system in a controlled release manner reduces the accumulation of drug and side effects by maintaining plasma blood level and also

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A REVIEW ON THE INCONSISTENT RELATIONSHIP BETWEEN CHOLESTEROL AND SUICIDE

HAARIKA B^{1*}, TEJASWI U² AND PUSHPASRI CH³

- 1: Department of pharmaceutics, Sarojini Naidu Vanita Pharmacy Maha Vidyalaya, 12-5-31/32, Vijayapuri colony, Tarnaka, Secunderabad, 500017, Telangana, India
- 2: Department of Pharm. D, Sarojini Naidu Vanita Pharmacy Maha Vidyalaya, 12-5-31/32, Vijayapuri colony, Tarnaka, Secunderabad, 500017, Telangana, India

*Corresponding Author: Dr. Balusu Haarika: E Mail: haarikabalusu09@gmail.com

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ABSTRACT

Cholesterol is a key component of the central nervous system, as it is required for cell membrane stability and proper neurotransmission. Any substance shows its biological effect with in normal range; exceeding the normal range or below the range shows unwanted effects, similar with the levels of body cholesterol levels. Many of the hypothesis came out to show that low levels of serum cholesterol in blood leads to suicidal and violent behaviour in mood disorders. Some of the studies have proven that low cholesterol levels lead suicidal attempt of individuals, as low cholesterol leads to improper uptake of serotonin and low membrane viscosity of brain which leads to mood depressive disorders and which further provokes to suicidal behaviour. Relationship between serum cholesterol and suicidality, on the other hand, have been questioned in recent years, based on the findings of a few recent studies that showed no link. However, the discussion over the link between cholesterol and suicide is still ongoing, and longitudinal studies including a larger sample of patients are needed to better elucidate this crucial subject. The objective of our paper is to assess the relationship between levels of serum cholesterol and individuals attempting suicide.

Keywords: Cholesterol, Suicide, Serotonin, Neurotransmission/Neuron communication,
Mood disorders





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DENDRIMERS - AN OVERVIEW ON TYPES AND APPLICATIONS

HAARIKA B*1, R. PRASANTHI² AND SREENIVAS N²

1, 2: Department of Pharmaceutics, Sarojini Naidu Vanita Pharmacy Maha Vidyalaya, 12-5-31/32, Vijayapuri colony, Tarnaka, Secunderabad, 500017, Telangana, India

*Corresponding Author: Dr. Balusu Haarika: E Mail: haarikabalusu09@gmail.com

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ABSTRACT

Dendrimers are nanosized, symmetrical molecules having a small atom which is surrounded by many symmetric branches known as dendrons. Dendrimers structure possesses the greatest impact on drug release. They grow outwards from core-shell that further reacts with monomers. These are having high compatibility with the biological systems. The presence of hyper branching, the well-defined spherical structure are the unique characteristics. These dendrimers are having a wide range of applications including medical and biomedical areas. Nano formulations based on dendrimers enhances solubility of low soluble drugs, arrives to the target tissue, enhanced bioavailability and havecontrolled drug release. In this review, we mainly focussed on the types of nanosystems, synthesis, classification and applications of dendrimers in drug delivery. Dendrimer structures which are synthesized by two different methods that are divergent and convergent growth methods.

Keywords: Dendrimers, Nano systems, Nano devices, Divergent and Convergent growth methods

INTRODUCTION

Nanotechnology is an emerging field of science that includes nanomaterials synthesis and development. Nanoparticles are defined as an objects ranging in size from 1 to100 nm. Nowadays different metallic nanomaterials are produced using

copper, magnesium, gold, zinc, titanium, alginate and silver. Nanoparticles can be synthesized both chemically or biologically. With chemical synthesis methods many adverse effects have been observed due to the presence of some toxic

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ORIGINAL ARTICLE



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Formulation and Evaluation of Liposomes Containing Erlotinib Hydrochloride

Zingade Sarika G¹, Nagoba Shivappa N.^{1*}, Swami Avinash B.¹, Vijayendra Swamy S. M.¹

¹Department of Pharmaceutics, Channabasweshwar Pharmacy College, Latur, Maharashtra, India. Email: nagobashivraj@gmail.com, nshivraj11@rediffmail.com *Corresponding Author

ABSTRACT

The aim of the present study is to formulate and evaluate liposomes containing Erlotinib hydrochloride. Erlotinib is a tyrosine kinase inhibitor which specifically inhibits epidermal growth factor receptors involved in angiogenesis of human non small cell lung carcinoma and inhibit growth of lung tumor. The present study conducted with the aim of preparing a site targeted nano-sized liposome to enhance the efficacy of Erlotinib which belongs to BCS class II. Total nine formulations were prepared by modified thin film hydration technique in which rotating flask contains glass beads for vortexing; lecithin (encapsulator), cholesterol (rigidator), and organic solvent. These formulations of liposome were evaluated and characterized for physical appearance, pH, drug content, % drug entrapment efficiency, microscopic determination and in vitro drug release. The results inferred F8 batch is most promising among all with highest drug entrapment i.e. 84.81% with drug release (~90%). Stability studies were conducted on optimized batch at 4° C, 40° C and room temperature for up to three months and formulation was found as stable at refrigerated temperature 4° C. **Keywords:** Liposome; Erlotinib; BCS class; Stability.

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INTRODUCTION

In 1960, Bangham introduced the liposome drug delivery; that phospholipids combined with water immediately formed a sphere and is capable of carry drug to the site of action [1]. Liposomes are concentric spherical vesicles of phospholipid bilayers having size 20- 1000 nm that are formed spontaneously in aqueous solution. The word liposome made of two Greek words, lipos (fat) and soma (body or structure). Lipid bilayered membrane encloses a central aqueous core of hydrophilic drugs while lipophilic drugs are entrapped within the bilayered membrane [2, 3].

Liposome bi-membrane is composed of natural and synthetic lipids, which are relatively biocompatible, biodegradable and non-immunogenic material. Because of amphipathic bilayer structure properties, liposomes are used as carriers for both lipophilic and water-soluble molecules. Liposomes have good biological properties of biocompatibility and biodegradability. They show promise as active vectors due to their capacity to enhance the entrapment performance by increasing drug solubility, and stability; delivering encapsulated drugs to specific target sites, and providing sustained drug release [4-6].

The liposomes help the drug to penetrate the cancer cells more selectively and decrease the possible side effects (nausea, hair loss and vomiting). Erlotinib is an EGFR-specific tyrosine kinase inhibitor which blocks the catalytic activity of the kinase responsible for non small cell lung cancer, thereby stopping complex network of downstream signaling pathway i.e. responsible for angiogenesis [7]. However, poor aqueous solubility and undesirable side effects limit the clinical application and local treatment of erlotinib. These side effects might be overcome by use of liposomes for tumor delivery and controlled release of erlotinib.

MATERIAL AND METHODS

Materials:

Erlotinib tosylate were obtained as a gift sample from Naprod life sciences Pvt. Ltd., Mumbai, India. Soyalecithin and HSPC gifted by Lipoid GMBH, Germany. Cholesterol were purchased from Research Lab Fine Chem Industries, Mumbai. The other chemicals, reagents and solvents used like potassium chloride,

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EFFERVESCENT FLOATING DRUG DELIVERY SYSTEM: A REVIEW

Haarika Balusu*1, Navya Mudapelly2, Sumana Donthula2 and Bhanu Priya Ch2

^{1,2}Department of Pharmaceutics, Sarojini Naidu Vanita Pharmacy MahaVidyalaya, 12-5-31/32, Vijayapuri Colony, Tarnaka, Secunderabad - 500017, Telangana, India

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ABSTRACT

In the recent years, scientific and technological advancements have been made in the research and development of novel drug delivery systems by overcoming physiological difficulty such as short gastric residence times and irregular gastric emptying times. Gastric emptying of dosage form is extremely variable process and ability to prolong and control the emptying time. Gastric transit time is valuable asset for dosage forms, which reside in the stomach for a long period of time than conventional dosage form. Many approaches at present uses the prolongation of the gastric residence times, including floating drug delivery systems, swelling and expanding systems, polymeric bio adhesive systems, modified shape systems, high density systems and other delayed gastric emptying devices. The drug from floating drug delivery systems can be absorbed in the upper parts of stomach, duodenum and jejunum. This is one of the best ideal approach for prolongation of gastric residence time of a drug for controlled and sustained release.

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INTRODUCTION

The oral route is the most suitable and widely used route for the delivery of drugs to the systemic circulation¹. Researchers keep studying about the drugs which show their action over an extended period of time, with a well-controlled release profile.

Even though it is less invasive, the real challenge is to increase the dosage in the gastrointestinal tract by increasing gastric residence time². The stomach and upper small intestine are main sites for drug absorption: prolongation of the residence time to achieve higher drug bioavailability, reduces the frequent administration of drugs, and shows better patient compliance³. Gastroretentive systems can remain buoyant in the gastric region for several hours which prolongs the gastric residence time of drugs. The controlled gastric retention of solid dosage forms was achieved by different mechanisms of mucoadhesion, sedimentation, flotation and by simultaneous administration of pharmacological agents that delay gastric emptying rate⁴. The most common convenient method of drug delivery is the oral route of drug administration. All these are the foremost commonly used dosage forms. They supply safe and convenient ways of active pharmaceutical ingredients (API) administration with excellent physicochemical stability ^{4,6}.

Gastroretentive Drug Delivery Systems

Gastro retentive dosage forms are drug delivery systems which remain in the stomach for an extended period of time and allow both spatial and time control of drug release. Basically, gastro retentive systems swells followingingestion and isretained in the stomach for more number of hours while it continuously releases the incorporated drug at a controlled rate to preferred absorption sites in the upper intestinal tract⁵. Their application can be advantageous in the case of drugs that are absorbed from the upper part of GIT and unstable in the alkaline medium of distal intestinal regions. Drugs that would benefit from gastro retentive drug delivery systems (GRDDS) are CNS drugs (Parkinson disease, epilepsy, Alzheimer and migraine), antiviral products (for HIV, herpes and hepatitis), certain antibiotics, antihypertensive drugs, anti-diabetic agents for Type II diabetes, drugs for local treatment of GI infections and gastric enzyme replacement ^{4,5}.

Drug Suitable For Gastro Retentive Drug Delivery System

- The drugs which are locally active in the stomach like antacidse.g. Misoprostol.etc
- Drugs showing narrow absorption window in gastrointestinal tract e.g. Riboflavin, furosemide, etc.
- Drugs showing instability in the colonic environment e.g. Ranitidine HCl, captopril.
- Drugs which are effective against normal colonic microbes e.g. Antibiotics against helicobacter pylori.
- Drugs which have low solubility at high pH values. e.g. Chlordiazepoxide, diazepam etc⁴.

Anchoring and Hydrophobic Nature of Coumarin in Newer Coumarin Based Chalcones: Synthesis, In Silico, and In Vitro Cell Viability Studies

Kannuri Rajeswari^a, Shireesha Manturthi^b, Kalam Sirisha^c, and Amar nath Velidandi^{a, 1}

^a Department of Chemistry, Chaitanya Deemed to be university, Telangana State, 506001 India
 ^b Department of Chemistry, National Institute of Technology Warangal, Telangana State, 506004 India
 ^c Department of Pharmaceutical Chemistry, Vaagdevi College of Pharmacy, Warangal, Telangana State, 506005 India
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Abstract—Coumarin is active pharmacophore; to enhance the activity of chalcone we inserted coumarin along with other cyclic groups. Fewer pyrazolone aldehydes produced using Wills Maeyer Haack reaction by grinding method. In alcoholic sodium hydroxide, cyclic ketones react with aldehydes to produce title compounds. To treat the ill cell a drug must be with a linker, anchoring group, and hydrophobic group. Herein, the enone group acts as a linker, the rings on both sides are connected, one side ring acts as the anchoring group, and the other side ring acts as the hydrophobic group; anchoring, hydrophobic dual roles played by coumarin ring. In this series, In silico studies results have shown that many compounds of this series potent for anti-cancer activity along with other biological activities, the In vitro cell viability studies of the series shows that, chalcone (I), (VIII), and (IV) are having IC_{50} values 2.96, 2.97, and 2.82 μ M against call 27 (or) oral cancer cell line.

Keywords: aldehydes, ketones, chalcone, coumarins, MTT assay

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INTRODUCTION

Chalcones serves as the starting material for number of key biological molecules. The biogenetic antecedents of flavonoids and isoflavonoids, which are plentiful in plants, are called chalcones [1]. Polyfunctionalized 3-benzylidenechromone-4 chalcone contained a novel series prepared, among them the majority of compounds have shown a good immune modulatory effect against various cancer cells and compared with the standard drug etoposide [2]. One molecule showed the highest (Tumor specificity) TS and (Potency—Selectivity Expression) PSE values among 15 chalcone derivatives, comparable to doxorubicin and methotrexate, respectively. Chemical modifications to the main molecule could be a viable option for developing novel anticancer medicines [3].

Malaria is a leading cause of death in endemic areas and the rise of drug-resistant parasites is concerning, powerful plant products have been identified. The synthesis of 10 chalcones with different substitutions, and evaluation of their antimalarial activity using chloroquine as a standard, reveals that cytotoxicity, and influence on hemozoin production [4]. Many of tocopherol-based compounds used for gene delivery

since they were designed and synthesized by differing in the head group region. Four distinct cell lines were tested for cytotoxity. The data is based on an average of three tests and indicates percentage of viability. The tocopherol-based heterocyclic formulations performed better in all four cell lines evaluated when compared to (Lipofectamine-2000) L2K [5]. A one-pot synthesis of newer 1,4-benzoxazine, 2,4-oxadiazole hybrids prepared from propanenitrile, and different aromatic carboxylic acids. In vitro anti-cancer activity of these compounds tested against four cancer cellines compared with etoposide [6].

Fourteen coumarin-derived compounds prepared and docking, molecular dynamics, and MM/GBSA studies shows that the molecule binds to the active rMAO-B site [7]. For global cancer control, efforts to develop a sustainable infrastructure for the spread of cancer prevention measures and the provision of cancer care in transitioning nations are crucial [8]. On the human hepatoma HepG2 cell line, the cytotoxicity of the decoction and individual plant extracts were assessed. The decoction has a substantial dose-dependent cytotoxic action, according to the results of MTT and SRB experiments [9]. Novel coumarin-pyridazine hybrid compounds with different polarizability and lipophilicity features were produced and evaluated against the two MAO isoforms, MAO-A and MAO-B,

¹ Corresponding author: e-mail: velidandi@yahoo.co.in.



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Synthesis, characterization and evaluation of thiopyrimidine derivatives as possible antimicrobial agents

J Bharath Kumar^{a,b}, I Rajyalaxmi^{a,c}, K Venkateshwarlu^a & K Sirisha*^a

^a Department of Pharmaceutical Chemistry, Vaagdevi College of Pharmacy Ramnagar, Hanamkonda 506 001, India
 ^b Pathfinder Institute of Pharmacy Education and Research, Mamnoor, Warangal 506 166, India
 ^c MLR Institute of Pharmacy, Dundigal, Quthbullapur, Hyderabad 500 043, India
 E-mail: venkataindica@yahoo.com; ragisirisha@yahoo.com

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A series of new thiopyrimidine derivatives have been synthesized *via* the reaction of Chalcones **3a-c** with thiourea to give the corresponding pyrimidine thiones **4a-c**. S-alkylation of pyrimidine thiones have resulted in novel 4,6-diaryl-2-alkyl thiopyrimidine **5a-i** derivatives. Molecular properties like number of hydrogen bond acceptors, number of hydrogen bond donors, volume, polar surface area, molar refractivity, number of rotatable bonds and drug likeness for synthesized compounds have been predicted by using different softwares such as Molinspiration, Molsoft and Chemsketch. The newly synthesized 4,6-diaryl-2-alkyl thiopyrimidine derivatives **5a-i** have been evaluated for their possible anti-microbial activity. Compounds **5b**, **5d** and **5e** have revealed significant activity against *E. coli*, *P. aerugenosa* (Gram +ve) and *B. subtilis*, *S. aureus* (Gram -ve) species while compounds **5a**, **5c**, **5f-i** are moderately active as compared to the standard drug Ciprofloxacin. Compounds **5c** and **5g** show potent anti-fungal activity against *Penicillium* species amongst the series in comparison to the standard Fluconazole.

Keywords: Chalcone, thiopyrimidine, S-alkylation, molecular properties, anti-microbial

Pyrimidine is one of the most important heterocycles exhibiting remarkable pharmacological activities. It contains two nitrogen atoms at positions 1 and 3 of the six-membered ring exhibiting a wide range of biological activities. Numerous methods for the synthesis of pyrimidine offer enormous scope in the field of medicinal chemistry^{1,2}. Condensed pyrimidine derivatives have been reported as anti-microbial, analgesic, antiviral, anti-inflammatory, anti- HIV, anti-tubercular, anti-tumor, anti-neoplastic, anti-malarial, diuretic, cardiovascular agents and hypnotic drugs for the nervous system, calcium-sensing receptor antagonists, adenosine receptor antagonists, etc.3 Thiopyrimidines (Figure 1) are broadly found in bioorganic and medicinal chemistry with applications in drug discovery and developments4. They are reported to possess broad spectrum of biological activities such as antibacterial, fungicidal, insecticidal, antihypertensive, tranquilizing, analgesic, antidiabetic, anticancer, etc.^{5,6} Recent reports revealed thiopyrimidine derivatives as platelet aggregation inhibitors and as selective inhibitors of CDK2 transferase⁷.

Thus, in view of their biological potential and to produce new molecules to combat the problem of drug resistance in microbial infections, some new thiopyrimidine derivatives have been designed in the present work based on our earlier studies on thiopyrimidines⁸. Herein, we report the synthesis and antimicrobial activity of some 4,6-diaryl-2-alkyl thiopyrimidines **5a-i**.

Results and Discussion

Chemistry

α,β-Unsaturated ketones (chalcones) **3a-c** have been prepared according to crossed aldol condensation by condensing aromatic/heteroaromatic methyl ketone **1** with different aromatic/heteroaromatic aldehydes **2** in dilute ethanolic sodium hydroxide solution at RT. Reaction of appropriate chalcones **3a-c** with thiourea and sodium hydroxide in ethanol produced thiopyrimidines **4a-c**. S-alkylation of thiopyrimidines **4a-c** using appropriate alkyl halides in presence of ethanolic sodium hydroxide solution *via* nucleophilic substitution reaction afforded 4,6-diaryl-2-alkyl thiopyrimidines **5a-i** (Scheme I).

Molecular Properties Prediction

Various molecular properties for synthesized compounds were predicted by using different softwares such as Molinspiration, Molsoft and Chemsketch⁹.



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A CASE REPORT ON SERUM CORTISOL INDUCED SIADH ASSOCIATED WITH SEVERE HYPONATREMIA

Dr. Mohammed Muneeruddin*¹, Poojitha Mutte², Divya Amara³, Tejaswi Uppala⁴ and Dr. Venu Talla⁵

¹Cluster–Clinical Pharmacologist, Medicover Hospitals, Madhapur, Hyderabad.

^{2,3,4}Pharm D. 6th Year, Sarojini Naidu Vanita Pharmacy Maha Vidyalaya, Tarnaka, Hyderabad.

⁵Head of Department of Pharm. D, Sarojini Naidu Vanita Pharmacy Maha Vidyalaya, Tarnaka, Hyderabad.

*Corresponding Author: Dr. Mohammed Muneeruddin

Cluster-Clinical Pharmacologist, Medicover Hospitals, Madhapur, Hyderabad.

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ABSTRACT

Cortisol production is reduced in primary adrenal insufficiency. Electrolyte imbalance develops in patients, which can be severe and life-threatening. We discuss the example of a 55-year-old male who was taken to the hospital with chief complaints of vomiting since 20 days. On evaluation the test results revealed chronic hyponatremia. The underlying reason was discovered to be primary adrenal insufficiency after further investigation. Our case study demonstrates that extreme hyponatremia can appear with neurological signs and symptoms. In the case of this patient, correction of hyponatremia, treatment with Tab. tolvaptan (Selective, competitive vasopressin receptor- 2 antagonist), Inj. ondansetron (Anti-emetic) and water restriction resulted in full clinical recovery.

KEYWORDS: Adrenal insufficiency, Cortisol, Hyponatremia, SIADH (Syndrome of inappropriate antidiuretic hormone secretion).

INTRODUCTION

Adrenal insufficiency (AI) is an illness in which adrenal cortisol production is either absent or insufficient. Direct adrenal insufficiency is the cause of primary AI (PAI), Secondary AI (SAI) is more common and is caused by disorders of the pituitary gland, whereas tertiary AI (TAI) is caused by diseases of the hypothalamus.^[1] It can

be life-threatening and its current prevalence is estimated to be between 100 to 140 instances per million, making it extremely rare. [2-3] Early detection of adrenal insufficiency is important to avert the potentially fatal consequences of severe hemodynamic and cardiovascular insufficiency. [4]

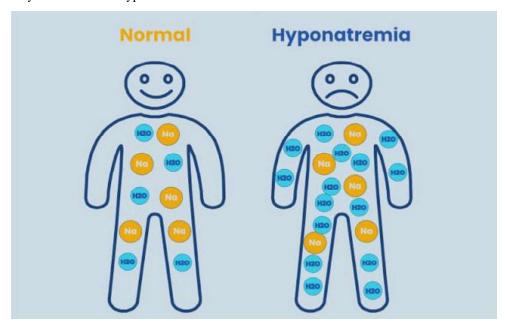


Figure: 1: Depiction of fluid and sodium content in hyponatremia.

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Case Study

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A CASE STUDY ON NOVEL AND CLASSIC ELEPHANT TRUNK **PROCEDURES**

Mohammed Muneeruddin¹*, Venu Talla¹, Divya Amara², Tejaswi Uppala² and Poojitha Mutte²

^{1*}Cluster – Clinical Pharmacologist, Medicover Hospitals, Madhapur, Hyderabad, 500018.

¹Head of Department of Pharm. D, Sarojini Naidu Vanita Pharmacy Maha Vidyalaya, Tarnaka, Hyderabad.

²Pharm D Intern, Medicover Hospitals, Madhapur, Hyderabad, 500018.

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*Corresponding Author Dr. Mohammed

Muneeruddin

Cluster - Clinical Pharmacologist, Medicover Hospitals, Madhapur, Hyderabad, 500018.

ABSTRACT

The elephant trunk procedure, in which a graft is inserted into a true lumen of distal aorta, is useful for closing the false lumen of the descending aorta. The open surgical treatment of an aortic disease (aneurysm or dissection) that affects the full length of the thoracic aorta is challenging surgically. However, H.G. Borst and colleagues found that with the classic technique (conventional arch replacement followed by descending aortic replacement), mobilization of the previous graft at the distal arch anastomosis was difficult and which might result in injury to the pulmonary artery, the aorta itself, the esophagus, and other nearby structures. As a consequence, they invented the Elephant Trunk approach in 1992, which Crawford and

Svensson later refined. The classic Elephant Trunk procedure, which has two stages, fits within this aggressive paradigm and allows for the rectification of coexisting or subsequent descending aortic dilatation. In 2003, the classic two-stage technique's novelty was advanced to one stage frozen elephant trunk technique which is a combination of stent and graft which will be inserted into the descending aorta followed by suturing into neck and other arteries that supply blood to heart and this procedure is associated with deep hypothermic circulatory arrest. Our study gives an overall description of 2 patients who underwent one-stage frozen elephant trunk procedure and two-stage classic elephant trunk procedure respectively.

KEYWORDS: Aorta, Aneurysm, Dissection, Lumen, Frozen.

ORIGINAL ARTICLE / ÖZGÜN MAKALE



TARGETTING THE 3BGQ - PIM1 KINASE INTERACTION WITH A SERIES OF NOVEL DITHIOCARBAMATE SUBSTITUTED 2OXOINDOLE DERIVATIVES - IN SILICO STUDIES

3BGQ - PIM1 KİNAZ ETKİLEŞİMİNİ HEDEF ALAN YENİ DİTİYOKARBAMAT İLE SÜBSTİTÜE 2-OKSOİNDOL TÜREVLERİNİN İN SİLİKO ÇALIŞMALARI

Muni Sireesha SUNKARA¹ , Dharani ANNEPALLY² , Donna Kanthi BITLA² , Sushma BOPPY² , Pallavi CHIDURALA² , Jhansi CHILUKA² , Saritha Jyostna TANGEDA^{2*}

¹Osmania University, Sarojini Naidu Vanita Pharmacy Maha Vidyalaya, Department of Pharmacoinformatics, 500007, Hyderabad, India ²Osmania University, Sarojini Naidu Vanita Pharmacy Maha Vidyalaya, Department of Pharmaceutical Chemistry, 500007, Hyderabad, India

ABSTRACT

Objective: Cancer is the major cause of mortality in most of the developing countries. Enormous chemotherapeutic agents developed are still need improvements in survival rates and quality of life for cancer patients. Pro-viral Integration site of Moloney murine leukemia virus (PIM1) is a family of serine/threonine kinase, regulated by calcium/calmudulin have been identified as a unique molecular target in oncogenesis. PIM1 has significant role in cell cycle regulation, cell survival, apoptosis, cellular senescence, drug resistance and it is emerging as a potential biomarker in number of human malignancies. Today many interesting PIM1 inhibitors are developed and few withdrawn from phase1 and 2 clinical trials, due to lack of bioavailability and toxicity. Hence the purpose of the present study is to develop more potent and less toxic compounds.

Material and Method: A series of novel 2-oxindoles with dithiocarbamates were designed as PIM1 inhibitors. All molecules were subjected to Molsoft, Molinspiration, Swiss ADME and pkCSM to predict their molecular properties which are important for drug candidate. Further, in order to find the binding affinity of designed molecules with PIM1 kinase protein and to rationalize their anticancer activity, molecular docking study was performed.

Result and Discussion: Results revealed that all designed compounds fulfilled the criteria for good oral bioavailability, low toxicity and the potential inhibitory activities. All of them were docked into active site of

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Corresponding Author / Sorumlu Yazar: Saritha Jyostna Tangeda *e-mail / e-posta*: sarithavanita13@gmail.com, Phone / Tel.: +919848928766

Recent advances in development of mek inhibitors – an update review

Navneetha Oleti, Shruti Deshpande and Saritha Jyostna T*

Masters in pharmaceutical chemistry (Department of Pharmaceutical Chemistry),

Sarojini Naidu Vanita Pharmacy Maha Vidyalaya, Osmania university, Tarnaka, 500017, Telangana, India.

Shruti Deshpande

Masters in pharmaceutical chemistry (Department of Pharmaceutical Chemistry),

Sarojini Naidu Vanita Pharmacy Maha Vidyalaya, Osmania university, Tarnaka, 500017, Telangana, India.

Saritha Jyostna T*

Professor (Department of Pharmaceutical Chemistry),

Sarojini Naidu Vanita Pharmacy Maha Vidyalaya, Osmania university, Tarnaka, 500017, Telangana, India.

*Address for Correspondence:

Dr. T. Saritha Jyostna,

Professor and Head.

Department of Pharmaceutical Chemistry.

Sarojini Naidu Vanita Pharmacy MahaVidyalaya,

Osmania University, Tarnaka, 500017, Telangana, India.

Abstract

Protein kinases are well known to orchestrate the activation of communication cascades in response to animate things and intracellular stimuli to manage cell proliferation and survival. The perturbation of such kinases by some mutation or abnormal macromolecule expressions has been closely associated to cancer. Drug development geared toward many targetable kinases might alter their participated pathways that are ready to trigger carcinogenesis. The present review is addressed on the role of mitogen-activated protein kinase (MEK) inhibitors in cancer treatment and their future importance in the treatment of various kinds of tumors.

Key words: Protein kinases, Serine threonine kinases, Carcinogenesis, MEK inhibitors

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DETERMINATION OF *IN-VITRO* ANTIBACTERIAL ACTIVITY OF NEEM AND NYCTANTHES FLOWERS

Pasupula Sri Varsha^{*1}, N. Shilpika², Shakapuram Neha³, Regula Shirisha³, Samruddhi Sapate³ and Shaik Saleem Uddin³

*1,2 Department of Pharmacognosy, Malla Reddy Pharmacy College, Maisammaguda, Hyderabad, Telangana, India. 3B. Pharm (Bachelor of Pharmacy) Malla Reddy Pharmacy College, Maisammaguda, Hyderabad, Telangana, India.

*Corresponding Author: Pasupula Sri Varsha

Department of Pharmacognosy, Malla Reddy Pharmacy College, Maisammaguda, Hyderabad, Telangana, India.

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ABSTRACT

Background: The term "antibacterial" refers to a substance, drug or chemical that can inhibit the growth of bacteria or destroy them completely. Antibacterial agents are most commonly used to treat bacterial infections in the human body, and to disinfect or sterilize surfaces. These agents work against both Gram positive and Gram negative bacteria. The crude extracts of cinnamon, garlic, basil, curry, ginger, sage, mustard, and other herbs also exhibit antimicrobial properties against a wide range of Gram-positive and Gram-negative bacteria. In the current study we have selected Neem and Nyctanthes flowers. Objectives: To Extract active constituents from plant materials (flowers) using suitable solvents by maceration process and comparing its Antibacterial activity shown in combinational plant extracts with that of single plant extracts. Methods: The flowers of Nyctanthes arbor-tristis and Azadirachta indica were collected, cleaned with water and dried and powdered. The dried plant material was subjected for extraction using ethanol for 7days, Dried and concentrated. The individual plant extracts and combined plant extracts were subjected for evaluation of Antibacterial activity using Agar cup plate method. Results and Discussion: The present study shows the ethanolic extracts of both Neem and Nycthanthes flowers containing phytochemicals showed synergistic anti bacterial activity when tested using in vitro method using Cefotaxime which is an Antibiotic used to treat a number of bacterial infections such as Pneumonia, lung infections, STD's (like Gonorrhea) etc.

KEYWORDS: Cefotaxime, Pneumonia, Gonorrhea, Anti bacterial activity.

INTRODUCTION

Bacteria are microscopic, single-celled organisms that exist by the millions, in every environment, both inside and outside other organisms. Bacteria are found almost everywhere on Earth and are vital to the planet's ecosystems.^[1]

In the human body, some bacteria play a major role in maintaining the health and function of the gastrointestinal tract. These are also known as gut flora or micro flora of the human body. It is estimated that the human body contains more bacterial cells than human cells.^[2]

Bacteria come under "Prokaryota" kingdom of the "Two Kingdom Classification". Prokaryotes are organisms that do not possess a defined nucleus or any other membrane bound organelles. They are considered to be the earliest forms of cells to exist on the Earth. There are various types of bacteria such as Sperical shaped (Eg: *Streptococcus group*), Rod shaped (Eg: *Bacillus anthracis or anthrax*), Spiral shape (Eg: *Treponema pallidum sps*). [1]

The term "antibacterial" refers to a substance, drug or chemical that can inhibit the growth of bacteria or destroy them completely. The "activity" of antibacterial drugs refers to the ability of the drug to show effect against bacterial growth/reproduction. These agents are most commonly used to treat bacterial infections in the human body, and to disinfect or sterilize surfaces. They work against both Gram positive and Gram negative bacteria.

The antibacterial agents act by inhibition of cell wall synthesis, inhibition of protein synthesis, Inhibition of Nucleic acid synthesis etc., and can be standardized by microbial assays such as Agar cup plate method, agar disk-diffusion method, agar well diffusion method etc.^[6]

The crude extracts like cinnamon, garlic, basil, curry, ginger, sage, mustard, and other herbs also exhibit antimicrobial properties against a wide range of Grampositive and Gram-negative bacteria.^[7]

Neem is an omnipotent tree and a sacred gift of nature mainly cultivated in the Indian subcontinent known by

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RESEARCH ARTICLE

OPEN ACCESS

Formulation and Evaluation of Polyherbal Cream in Acne Treatment

Nasreen Begum, G.Rakesh, K.Shirisha, P.Srivarsha, N.Shilpika* Malla reddy Pharmacy college, Maisammaguda, Secunderabad.

Corresponding author:
Shilpika Nagula
Malla Reddy Pharmacy College, Maisammaguda, Secunderabad
Email: shilpika047@gmail.com

ABSTRACT:

Acne vulgarisis the majorly widespread skin problem of pilosebaceous that has an effect on regions with large oil glands, like on face, trunk, andback. Acneis commonly has the formation of inflammatory seborrhea, come done and lesions. Propionibacterium acnes and Staphylococcus epidermidis cause pus in acne resulting in inflammation. Our research is deliberated to evaluate antimicrobial potential of plants from the claims of folks. Antibacterial activity of poly herbal anti-acne cream containing the plant extracts of Achyranthesaspera (leaves), Catheranthusroseus (leaves), Lini semen (seeds) which were extracted out by maceration process using ethanol solvent. The antibacterial potential of ethanol extract of Achyranthesaspera, Catheranthusroseus, Lini semenwas used to prepare an anti-acne cream, to determine its activity using agar cup plate method. The antibacterial activity of the series of dilutions of each plant extract was compared with the standard drug Ampicillin against propionibacterium. The result of antibacterial action of the polyherbal cream gave greater zone of inhibition (ZI) in comparison with single plant extract. Therefore, it can be accentuated that the formulated poly herbal anti-acne cream has potential antibacterial effect against propionibacterium in the treatment of acne which is the common bacteria in causing acne. The polyherbal antiacne cream prepared also conceded all the pharmaceutical evaluation parameters.

Keywords: Antiacne cream, polyherbal extract, Achyranthesaspera, Catheranthusroseus, Lini semen

INTRODUCTION

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Acne vulgaris has become a never-ending inflammatory skin problem of *pilosebaceous* that affects face, back, and trunk ^[1]. It is more or less a universal disorder happening to races and touching 96% of boys and 84% of girls. Acne is a big problem in the teenage and of course effects all the age groups. It decreases the confidence levels in the individuals and also result in physiological problems. Most of the population effects with acne do not go for the treatment, but it show be treated in a right way in the right time and with a right drug. In this study we came up with an indeginous medicine which is very effective in the treatment of acne with very minimal side effects. ^[2-5]

Acne vulgaris results in seborrhea, comedone, inflammatory lesions and presence of bacteria *Propionibacteriuacnes*, *Staphylococcus epidermidis and Staphylococcus aureus* in the follicles andin sebum^[2]. *P. acnes*is a obligate anaerobic bacteria. It concerns the growth of inflammatory acne by its ability to turn on complements and to break down sebaceous triglycerides into fatty acids, which migrate





Design, synthesis and molecular docking study of thiophenyl hydrazone derivatives as tubulin polymerization inhibitors

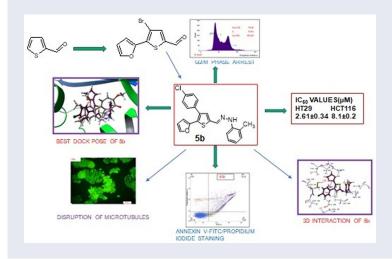
Vinutha Kuchana^{a,b}, Vaeshnavi Kashetti^b, Saritha Jyotsna Tangeda^a, and Vijjulatha Manga^b

^aDepartment of Chemistry, Sarojini Naidu Pharmacy Maha Vidyalaya, Osmania University, Hyderabad, India; ^bDepartment of Chemistry, University College of Science, Osmania University, Hyderabad, India

ABSTRACT

A series of thiophene derivatives substituted at 2, 3 and 5 positions were designed and synthesized using 2,3-disubstituted thiophene aldehyde and alcohol as key building blocks. Invitro cytotoxicity assessed against PC-3, DU145 (prostate), A549 (lung), HT29, HCT116 (colon), MCF7, MDAMB231 (breast), B16F10 (melanoma) NCI (Colorectal) cancer cell lines by conducting (MTT) assay of thiophene derivatives. Most of these synthesized compounds showed anti-cancer activity, compound ${\bf 5b}$ showed good cytotoxicity with IC $_{50}=2.61\pm0.34\,\mu\text{M}$ on HT29 cell line. Also, the key property of cell migration was observed while treating cells with ${\bf 5b}$. The Cell cycle arrest at G2/M phase was observed by ${\bf 5b}$ on HT29 cell line which inhibited tubulin polymerization with IC $_{50}$ value of $8.21\pm0.30\,\mu\text{M}$. Moreover, binding pose with co-crystal ligand and interaction with colchicine binding site of ${\bf 5b}$ was established by molecular docking studies. Hence this scaffold can be developed as anti-cancer agents that target tubulin polymerization.

GRAPHICAL ABSTRACT



ARTICLE HISTORY

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KEYWORDS

Annexin-V binding assay; cytotoxicity analysis; G2/M arrest; Hydrazones; molecular docking

CONTACT Vijjulatha Manga vijjulathamanga@gmail.com Department of Chemistry, University College of Science, Osmania University, Hyderabad 500001, India.

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PHARMACEUTICAL SCIENCES AND RESEARCH



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IN-VITRO ALPHA-AMYLASE AND ALPHA-GLUCOSIDASE INHIBITORY ACTIVITIES OF POLYHERBAL FORMULATION

Asma Fathima, Anusha Dev and Praneetha Pallerla *

Sarojini Naidu Vanita Pharmacy Maha Vidyalaya, Osmania University Secunderabad - 500017, Telangana, India.

Keywords:

Alpha amylase, Alpha glucosidase, Diabetic complications, IC₅₀

Correspondence to Author: Praneetha Pallerla

Sarojini Naidu Vanita Pharmacy Maha Vidyalaya, Osmania University Secunderabad - 500017, Telangana, India.

E-mail: asma.fathima49@gmail.com

ABSTRACT: Diabetes mellitus is a chronic disease identified as hyperglycemia that occurs either when the pancreas does not produce enough insulin or when the body cannot metabolize its insulin. Insulin is a hormone that regulates blood sugar levels. Hyperglycemia, or raised blood sugar, is a common effect of uncontrolled diabetes and, over time, leads to serious damage to many of the body's systems. Alpha-amylase and alphaglucosidase inhibitors are used to achieve greater control over hyperglycemia in type 2 diabetes mellitus. In the present study, the methanolic extract of leaves of Azadirachta indica, Murraya koenigii and Psidium guajava were prepared by maceration. The methanolic extracts of leaves of Azadirachta indica, Murraya koenigii and Psidium guajava were mixed in equal proportions to form a polyherbal extract and studied for *in-vitro* alpha (α)amylase and alpha (α)-glucosidase inhibitory activities. In alpha-amylase activity, alpha-amylase solution (0.5 mg/mL) and substrate, 1% starch was used and the absorbance was measured at 540nm. In Alpha-glucosidase activity, alpha-glucosidase (0.5 mg/mL) and substrate, 5 mM p-nitrophenylalpha-D-glucopyranoside was used and the absorbance was recorded at 405 nm. Different concentrations of the polyherbal formulation were assessed for alpha-amylase and alpha-glucosidase inhibitory activities with an IC₅₀ value 5.2 μg/ml and 5.98 μg/ml extract, respectively, and were well comparable with the standard drug, acarbose. The polyherbal formulation exhibited significant alpha-amylase and alpha-glucosidase inhibitory activities in dosedependent manner and was comparable to that of standard drug, acarbose.

INTRODUCTION: Diabetes mellitus is a primary metabolic disorder of carbohydrate metabolism characterized by elevated blood glucose levels (hyperglycemia). Different classes of diabetes have been identified type 1, type 2, gestational diabetes, and specific types of diabetes due to other causes *e.g* monogenetic diabetes syndrome.



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Diabetes results from insufficient production of the hormone insulin (type1 diabetes) or an ineffective response of cells to insulin (type 2 diabetes). This disarray in metabolism leads to micro-and macro-vascular changes causing secondary complications including heart attack, stroke, kidney failure, leg amputation, vision loss, and nerve damage ¹.

Among 7.7 billion total populations (2019), around 463 million adult people have diabetes, with a global prevalence of 9.3%, and may rise to 10.9% by 2045 ². The proportion of people with type 2 diabetes is increasing in most countries and 374 million people are at increased risk of developing



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CO-CRYSTAL TECHNIQUE OF SOLUBILITY ENHANCEMENT COMPREHENSIVE **REVIEW**

Mayuri Kondapalli¹*, Shravasti Banoth², Sai Priya Bairagoni³ and Hyma P.⁴

Sarojini Naidu Vanitha Pharmacy Maha Vidyalaya, Hyderabad, Telangana, 500017.

*Corresponding Author: Mayuri Kondapalli

Sarojini Naidu Vanitha Pharmacy Maha Vidyalaya, Hyderabad, Telangana, 500017.

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ABSTRACT

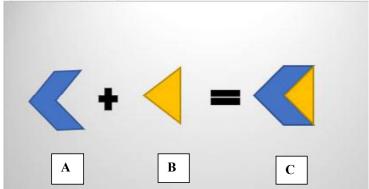
Co-crystal is a unique crystalline material containing two molecular components solid at room temperature having defined stoichiometric ratio. For administration of high doses of drugs such as HIV/AIDS, tuberculosis and other cocrystal are drug combination strategies used for the treatment and management of drug resistance and adverse reactions Improving the various parameters of a drug molecule such as solubility, melting point, pharmacokinetic, pharmacodynamic and bioavailability is possible through co-crystals. Various validation instruments such as x-ray diffraction and differential scanning calorimetry gives the overview of qualitative and quantitative aspects of cocrystals and evaluation of co-crystals. Attention of co-crystals in the discovery plays a role in drug design and development. A complete case study of theophylline and 5-nitrouracil regarding co-crystal. methodology and overview and methods of preparation of co-crystal.

KEYWORDS: Pharmaceutical Co-Crystal, Conformer, 5-Nitrouracil, Theophylline, Physicochemical properties.

INTRODUCTION

In 1894, Friedrich Wohler solved 1st cocrystal structure i.e., quinone and hydroquinone, but that is succeeded in the present century. In supramolecular chemistry cocrystal played a major role for the field of pharmaceutical, chemical and regulatory agencies. [2] As the efficacy of the active pharmaceutical compounds physicochemical depends on the properties/ pharmacokinetic and pharmacodynamic properties like solubility, Hygroscopic, dissolution, stability, bioavailability. [2,3] Cocrystal is a multiple component crystal of salts contributes key role in pharmaceuticals. [4] Accordingly to different literatures co-crystal develops a better drug product with a best and effective physicochemical product that does not change the pharmacological activity of the active pharmaceutical ingredient. Co crystallization possess the greater therapeutic activity. Two (or) more molecules together within a crystalline lattice that are non-turbulent are so called co-crystals. Solvates and hydrates are also included in co-crystals.^[4,5]

Screening processes of crystallization process



- A Active pharmaceutical ingredients.
- Conformers В
- Cocrystal



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A REVIEW ON INVITRO ANTICANCER EVALUATION STUDIES

KYATHAM RAMADEVI, RAJU BATHULA, HEMALATHA SATTU

- School of Pharmacy, Anurag University, Venkatapur, Ghatkesar, Hyderabad, T.S, India.
- ²Netaji Institute of Pharmaceutical Sciences, Toopranpet, Choutuppal, Yadadri, T.S, India

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ABSTRACT

Cancer is one of the world's most pressing health care challenge with more than 14 million people diagnosing each year. New insights into cancer and inhibition of its regulators will be investigated for the development of a novel treatment for cancer. The present research aimed to Cytotoxic Evaluation of New chemical Derivatives. Cancer is leading to 13% deaths in the world, as per the World Health Organization (WHO) survey the Oncological patients count may increase to 21.7 million cases and 13 million deaths by 2030.

Keywords: Cancer, Cytotoxic Evaluation, Oncological Patients.

INTRODUCTION

Cancer Cells:

- Cancerous cell division goes repeatedly out of control even though they are not needed, the cancer cells crowd out other healthy cells and make them function abnormally.
- They can likewise decimate the working of significant major organs.
- Mutation of a normal gene is the cause to change in deoxyribonucleic acid sequence.

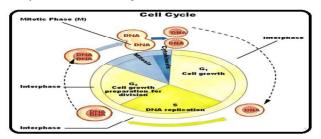


Fig: 1. The process of cancer cell division

*Corresponding author: Dr Raju Bathula

Head of the Department

Department of Pharmaceutical Analysis, Netaji Institute of Pharmaceutical Sciences, Toopranpet, Choutuppal, Yadadri, T.S, India.-500088.

Email: dr.rajubathula@gmail.com

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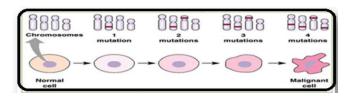


Fig: 2. The Process of the Normal gene after several mutations produces Mutated Genes (Oncogenes) and these mutated genes cause to cancer.

CARCINOGENS:

Cancer-causing is also called carcinogens and these are the following examples.

- Ionizing radiations like UV light, X Rays etc.
- Chemicals like Tar from Cigarettes, Natural or Synthetic Chemicals.
- Virus infections like Cervical Cancer caused are by Papilloma Virus.

Those tumours which do not spread from their site of origin and can crowd out surrounding cells are called Benign Tumours.

Ex: a brain tumour, warts etc.

Those tumours which can spread from the original site and cause secondary Tumours are called Malignant Tumours. These metastatic tumours are interfering with neighbouring cells and block the blood vessels, Gut, glands, lungs etc.

ANGIOGENESIS:

• The cells need huge amount of nutrients to sustain the rapid growth and division of the cells. In order to grow beyond 2mm

³ Sarojininaidu Vanitha Pharmacy Mahavidyalaya, Tarnaka, Secunderabad, T.S, India

Case Report



A Case Report on Transvaginal Septum Manifested by Haematocolpus

Dr. Rishitha Sanjana Abbagoni*, Dr. Aakaram Sujala

Assistant Professor, Pharm-D Department, Sarojini Naidu Vanitha Pharmacy Mahavidyalaya, Tarnaka, Secunderabad, Telangana, India.

*Corresponding author's E-mail: arsanjana1526@gmail.com

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ABSTRACT

Transvaginal septum is a rare congenital vaginal anomaly in which a thick fibrous tissue runs transversely in vagina, dividing Vagina into upper and lower cavities. Haematocolpus is a gynaecological condition and is usually referred to as vaginal accumulation or obstruction of menstrual blood, and is usually caused when there is no way for the menstrual blood to flow out such as in case of transverse vaginal septum. The prevalence of Transverse vaginal septum condition is at 1 per 70,000 females. Most of the time transverse vaginal septum goes unnoticed or undiagnosed until a female reaches her menarche when she presents to the clinic with the symptoms of cyclic abdominal pain, amenorrhea, menorrhagia, difficulty during mating and sometimes with the problems of difficulty micturition. The diagnosis can be done by careful history taking, gynaecological examination. Sometimes additional imaging tests such as ultrasound and MRI can be performed to obtain in detail information of the condition. Treatment for transverse vaginal septum associated with or without haematocolpus usually depends upon surgical excision of the septum. A 14-year-old girl presented to the clinic with the chief complaints of cyclical abdominal pain with amenorrhoea and difficulty to pass urine. Upon careful physical examination the girl was diagnosed with transverse vaginal septum associated with haematocolpus. Treatment done was incision and drainage of haematocolpus with marsupialisation under general anaesthesia. Patient was discharged upon finding no development of any events post-surgery and was followed for six months and was found to have normal menstrual cycle with no other complications. Transverse vaginal septum is a rare congenital genetic anomaly and sometimes haematocolpus is the manifestation where surgery is the immediate procedure to be done to prevent any further complications and to preserve the normal menstrual and reproductive functions.

Keywords: Transvaginal septum, Haematocolpus, Vaginal anomaly, Amenorrhea, Menorrhagia.

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INTRODUCTION

ransvaginal septum is a rare congenital utero-vaginal anomaly obstructing vagina and affecting every 1 in 70,000 females ^{2,3}. Transvaginal septum might be of either perforated (incompletely closed) or imperforated (completely closed) and can form at any part of the vagina i.e., either in upper part or central part or lower part of the vagina ^{1,3}. However, the reported approximate prevalence rates in terms of where the septum can form in vagina are found to be at 46% in upper vagina, 40% in central part of the vagina and 14% in lower part of the vagina 2,3. In this condition a thick fibrous tissue called as septum runs across vagina longitudinally dividing the vagina into lower and upper cavities 3,10. In imperforate septum cases, the septum causes an obstruction for the free outflow of menstrual blood leading to a condition called as haematocolpus or hematometra 1. Haematocolpus is a condition in which menstrual blood gets collected or obstructed in the vagina due to either imperforate hymen

or vaginal septum 1. The exact cause for this congenital anomaly is not known, but combination of multiple factors such as in-utero exposure to some agents or autosomal recessive inheritance might be the possible expected causes^{5,11}. However, the development of septum is said to occur during embryogenesis when Mullerian ducts and urogenital sinus do not fuse properly leading to vaginal obstruction ^{1,5,6,9}. The symptoms of transvaginal septum does not show up until a girl reaches her puberty or menarche as the condition is manifested by primary amenorrhea (in case of imperforate septum) or menorrhagia (in case of perforate septum), lower abdominal pain, cyclic abdominal pain, difficulty urinating, difficulty in mating and constipation 1,2,9,10. Diagnosis of this condition always possess a challenge due to the absence of signs and symptoms until menarche and its resembles with other health problems due to which it often gets misdiagnosed ^{6,8}. However, proper medical history taking with careful physical, gynaecological examination helps to detect the condition and performing imaging tests such as Ultrasound and MRI would provide confirmation and in depth information about the condition such as exact location, thickness of septum and presence or absence of haematocolpus 1,2,3,7,8. Treatment or approaches to treat transvaginal septum completely depends upon the type, thickness and location of the septum, a patient is having ^{2,5}. In case of a small septum, vaginal dilators can provide the solution, but in case where







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Original Article

FORMULATION AND EVALUATION OF ORAL FAST DISSOLVING FILMS OF NAPROXEN SODIUM

HYMA P., SAKEENA FATIMA*

Department of Pharmaceutics, Sarojini Naidu Vanita Pharmacy Maha Vidyalaya, Secunderabad, Telangana, India Email: sakeenafatima153@gmail.com

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ABSTRACT

Objective: The aim of this investigation was to prepare ODFs containing Naproxen Sodium, an NSAID, using solvent casting method and to evaluate them to put together a dosage form which can be taken without water, is easy to administer, has a rapid onset of action and can surmount first pass metabolism. Six distinct formulations of naproxen sodium ODF (F1-F6) were created in this investigation by varying the quantity of croscarmellose sodium, a super disintegrant.

Methods: Naproxen Sodium ODF's were prepared by solvent casting method. Evaluation of prepared ODF's was done by considering various parameters such as film thickness, folding endurance, disintegration time, surface pH, weight variation, *in vitro* dissolution test, content uniformity and FTIR.

Results: F6 has shown to be the best fast release formulation in terms of disintegration time (less than 1 minute) and dissolution (103.5 % after 30 min). Formulation F6's other film characteristics, such as weight variation, thickness, pH, and folding endurance, were all within the USP limit.

Conclusion: By virtue of quick disintegration self-administration without water or chewing, oral fast dissolving film (OFDF) is one such new technique to enhance consumer acceptance. The film is an excellent intraoral fast-dissolving medication delivery method by which a wide range of medicines, including neuroleptics, cardiovascular drugs, analgesics, anti-asthmatic, antihistamines and drugs for erectile dysfunction, can be manufactured. From the standpoint of the patient, oromucosal medication delivery is appealing since it allows for easy administration without the need to swallow, as well as better patient safety. As a novel delivery mechanism, the notion of a quick-dissolving dosage form has gained popularity. By lowering dose frequency, this method will deliver optimum therapeutic efficacy, improved bioavailability, and maximum stability. This will also surmount first-pass metabolism of drugs. This method allows for faster medication absorption from the pre-gastric region, perhaps resulting in a faster onset of action.

Keywords: ODF, Patient compliance, Naproxen sodium, Super disintegrant, Surmount first pass

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INTRODUCTION

Drug delivery methods alter the profile of a drug's release, absorption, distribution, and elimination in order to improve product efficacy, safety, and patient comfort and compliance. Because of its versatility, the convenience of use, and painlessness, as well as patient compliance, the oral route of administration is regarded the most frequent route for systemic medication effects [1, 2]. In terms of flexibility, fast dissolving films are the most advanced solid dosage form. Orally dissolving films (ODFs) are a type of oral drug delivery system that was developed based on transdermal patch technology [3]. Orodispersible film (ODF) has recently received increased interest because of its particular advantages for target populations such as toddlers and the elderly who have trouble swallowing [4].

These films might include soluble, insoluble, or taste-masked pharmacological compounds. Aqueous polymer matrices with a wide molecular weight range are commonly used in the film's formation, aiding in the achievement of specific physical properties. Selecting appropriate polymer types to fulfill specific API loading demands and rate of dissolution might result in tailormade properties [5]. Polymer that dissolves in water, medicine, plasticizer, surfactant, sweetener, colors, flavors and saliva stimulating agents are some of the common ingredients in ODF's. The polymer is a key component of the oral film; it serves as the backbone that retains and regulates the drug's release. The use of super disintegrants is the most common method for producing fast dissolving films [6]. pH modifiers have been suggested as a viable method for enhancing the dissolution and bioavailability of medicines with pH-dependent solubility. A pH modulator might change the drug particles' microenvironmental pH to one that facilitates drug breakdown [7].

A very thin oral strip is put on the patient's tongue or any other oral mucosal tissue as part of the delivery system. The strip is instantaneously moistened by saliva, and the film quickly hydrates, disintegrates and dissolves to release the medicine for oromucosalabsorption [8]. As a result, the oral mucosa is an appealing location for drug administration [9].

These dosage forms are useful in patients who have an active lifestyle, such as pediatrics [10], geriatrics, bedridden, emetic patients, diarrhea, acute allergy reactions, or coughing. Oral disintegrating dosage forms provide an extra benefit in the treatment of individuals with mental illnesses. FDOFs are also beneficial when a local anesthetic, such as for toothaches, mouth ulcers, cold sores, or teething, is required. For the systemic distribution of active pharmaceutical ingredients (APIs) for overthe-counter (OTC) medicines, ODF's are given intraorally.

Advantages

ODFs have numerous advantages, including the convenience of use for pediatricians [10] and the fact that they do not require water for ingestion-a useful feature for patients who travel. They have a pleasant tongue feel, which helps to modify people's perceptions of the drug as bitter, especially in children. As saliva travels down into the stomach, certain medicines may be absorbed from the mouth, throat, and esophagus, increasing drug bioavailability. These vanquish the hepatic first-pass metabolism [11], resulting in increased bioavailability and a decrease in dosage. The risk of suffocating or choking while using traditional solid formulations is eliminated, resulting in increased safety. When a quick start of action is necessary, ODFs come in handy. Because the medication is in a solid-state until it is ingested, ODFs maintain their stability for longer periods of time. As a result, ODFs combine the benefits of solid dosage forms in terms of stability and



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Review Article
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EMULGEL – AN INNOVATIVE MODUS OPERANDI FOR FORMULATION OF HYDROPHOBIC DRUGS FOR THE TREATMENT OF DERMATOLOGICAL DISEASES

Lingam Harini^{1*}, Madappa Vaishnavi¹, Kothuri Jyothi¹, Kulthe Geetha¹ and Hyma Ponnaganti²

¹Department of Pharmaceutics, Sarojini Naidu Vanita Pharmacy Mahavidyalaya, Vijaypuri Colony, Tarnaka, Hyderabad 500007, Telangana.

²Associate Professor, Department of Pharmaceutics, Sarojini Naidu Vanita Pharmacy Mahavidyalaya, Vijaypuri Colony, Tarnaka, Hyderabad 500007, Telangana.

*Corresponding Author: Lingam Harini

Department of Pharmaceutics, Sarojini Naidu Vanita Pharmacy Mahavidyalaya, Vijaypuri Colony, Tarnaka, Hyderabad 500007, Telangana.

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ABSTRACT

In this cutting-edge era, there have been a lot of advancements in the medical field to improve the health of individuals suffering from a wide range of diseases either caused by invading microorganisms or by abnormal functioning of body organs. One such example is the formulation of Emulgel, which is a type of topical gel, known to have greater absorptive and therapeutic properties when compared with liquid and solid dosage forms. The main principle applied in the preparation of Emulgel is the incorporation of transparent gel into the emulsion as a means to diminish the adverse effects of dermatological diseases. The amalgamation of an emulsion into gel gives it more stability and henceforth is gaining more popularity as a topical drug delivery system with the sustained-release property as well, in which the drug is released slowly with a specific time interval to give efficient and long-lasting action, along with it can also incorporate hydrophobic drugs, which is a major limitation observed in gel-based formulations. Eventually leads to an opportunity to cure dermatological diseases caused by viruses as well and not only constricted to bacteria or fungal infections.

KEYWORDS: emulgels, hydrophobic drugs, skin, topical gel, drug delivery, in-vitro.

INTRODUCTION

The phenomenon, in which a drug-containing formulation is directly delivered into the systemic circulation when applied to the surface of the skin to cure dermatological ailments, is known as transdermal drug delivery. This path shows a greater therapeutic effect for local and systematic treatment respectively.^[1] Skin is the largest organ in the body and acts as an easier accessible target for remedial treatment and diagnosis of hypodermal infections. Topical drug delivery is specifically used when other routes of administration do not seem to function properly with a major disadvantage being first-pass metabolism with oral formulations and risks associated with intravenous/subcutaneous/intramuscular administrations. There are other major drawback occurrences such as gastric emptying rate, pH changes, enzymes metabolism and ADME changes which are repressed by the topical drug delivery system making it an advantageous drug release pathway. [2] Emulgels are a form of a dosage form in which gel and emulsion are combined to give a more therapeutic effect when compared with the traditional ointment form. Emulsifiers and thickeners are employed in the formulation of emulgel, as their gelling capacity allows the formation of stable emulsion with a better

surface, interfacial tensions and viscosity characteristics. These days, transparent gels are highly in use for the formulation of emulgel as they entrap large amounts of aqueous or aromatic liquid in a network of colloidal solid particles, which may consist of inorganic salts such as aluminium or organic polymers, permitting greater dissolution and migration of drugs into the systemic circulation. Even though gels have many advantages such as being thixotropic, greaseless, cleansable, spreadable, higher shelf-life and non-staining, delivery of hydrophobic drugs becomes immensely difficult because gels are hydrophilic. [4]

Hence gel and emulsion are incorporated together to overcome this problem so that hydrophobic drugs can also be formulated in gel form for the finest and optimum action.

Composition of the skin

A part of topical drug delivery is also associated with transdermal applications for treating specific dermatological problems such as eczema, herpes labialis and dermatitis. To create an efficient formulation, an understanding of skin anatomy and its physiology is of the utmost requirement. The skin of a healthy adult

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COMPREHENSIVE REVIEW ON ISOXAZOLE ANALOGS – VERSATILE SCAFFOLD WITH SYNTHESIS AND BIOLOGICAL POTENTIALS

Authors: Pranitha Balasani¹, Neha Patil¹, Ambika belekara¹, Hemalatha Sattu^{*}

[1] Department of pharmaceutical chemistry, sarojini naidu vanita pharmacy maha vidyalaya, vijayapuri colony, Tarnaka, Secunderabad-500017, Telangana, India.

*Corresponding author: Dr.S. Hemalatha, HOD and professor, department of pharmaceutical chemistry, sarojini naidu vanitapharmacymahavidyalaya, Tarnaka, Secunderabad -500017, Telangana, India.

Abstract:

Isoxazole is the compound with 5-membered heterocyclic ring that has wide spectrum in many pharmacological activities such as Anti-cancer, Anti-inflammatory, Anti-tubercular, Anti-Microbial, Anti-oxidants. The outstanding chemotherapeutic profile of isoxazoles, they are engaged in presiding is that they procure distinctive properties of an aromatic structure but consists of weak nitrogen and oxygen bond which under basic and reducing conditions, it is a capable site of ring cleavage. As the ring system stability allows the exploitation of substituents to produce effective complex derivatives, the isoxazoles are very useful imtermediates. The substituted Isoxazoles offered a extremity that possess notable biological potency. There are various synthetic approaches to position in medicinal chemistry reasearch and industry. The characteristic feature of these heterocycles establish the isoxazole ring, the major method of synthesizing the isoxazole is 1, 3-dipolar cyclo-addition of alkenes and alkynes. Allowing the huge research on isoxazoles, this review comprehend the various biological activities of isoxazole derivatives and synthetic methods for isoxazole derivatives. To conclude, it will be useful for new drug discovery that contains isoxazole moiety.

Keywords: isoxazole, Anti-cancer, Anti-tubercular, Heterocyclic.

I.INTRODUCTION

Heterocyclic compounds have charmed noticeable attention as they interpret the link between chemical and life-sciences^[1]Heterocycles that contain nitrogen and oxygen atom are regarded as an chief class of compounds in medicinal chemistry due to their applications. The five-membered compounds that contains 'O' and 'N' in 1&2 positions is known as isoxazole^[2]



fig.1- structure of isoxazole

The isoxazole ring was first synthesized by Dunstan and Dymand. The chemistry of isoxazole is developed in between 1930-1946. The study is contributed from Quilico's studies from nitrile oxides and un-saturated compounds. The common name for 5- membered unsaturated heterocycles as isoxazole was primitively put forwaded by Hantszch [3]. In the past decades, noticeable endeavours were concentrated on the synthesis of isoxazoles due to their functions [4]. The synthesis of isoxazole ring method which is majorly used is 1,3 dipolar

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Research Article

IN-VITRO ANTIDIABETIC ACTIVITY OF STANDARDIZED ACAIBERRY EXTRACT

Praneetha Pallerla*, Harshitha Posani

Sarojini Naidu Vanitha Pharmacy Maha Vidyalaya, Tarnaka, Hyderabad, Telangana State, India
*Corresponding author: drppallerla@gmail.com

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ABSTRACT

In the present study, the standardized Acaiberry extract was studied for in-vitro antidiabetic activity. The aim of this work was to evaluate the inhibitory activities of the methanolic extract of standardized Euterpe oleracea (Acai berry) of family Arecaceae, at different concentrations. Diabetes is a severe, metabolic disorder characterized by increased levels of glucose that circulates in the blood plasma. Alpha amylase and alpha glucosidase inhibitors are used to achieve greater control over hyperglycemia in type 2 diabetes mellitus. The present study intends to screen alpha amylase and alpha glucosidase inhibitors from natural sources like plants in order to minimize the toxicity and side effects of the inhibitors currently used to control hyperglycemia. The acaiberry extract exhibited significant α -amylase and α -glucosidase inhibitory activities with IC₅₀ value 6.29 mg/ml and 7.03 mg/ml respectively and well compared with standard Acarbose for alpha (α)-amylase and alpha (α)-glucosidase inhibitory activities respectively.

Keywords: Acaiberry, Acarbose, Alpha amylase, Alpha glucosidase.

1. INTRODUCTION

Diabetes is a severe, metabolic disorder characterized by increased levels of glucose in blood that causes damage to the heart, blood vessels, eyes, kidneys and nerves overtime. Type 2 diabetes is the most common disorder which is prevalent in adults, and occurs either due to resistance to insulin or insufficient production of insulin in the body [1]. Millions of people worldwide have diabetes, the majority living in low-and middle-income countries, and 1.5 million deaths are directly attributed to diabetes each year [2]. Among 7.7 billion total population (2019), around 463 million adult people have diabetes with a global prevalence of 9.3% and may rise to 10.9% by 2045 [3]. The conventional treatments for type 2 diabetes include the reduction of the demand for insulin, stimulation of endogenous insulin secretion, enhancement of the action of insulin at the target tissues and the inhibition of degradation of oligo- and disaccharides [4]. The distinct digestive enzyme in saliva is α -amylase. It hydrolyses α -1,4glycosidic linkages in starch to yield maltose and glucose which results in increased glucose levels. The α -amylase inhibitors play a vital role in delaying the glucose absorption rate in the body thus reducing the serum blood glucose levels in diabetic individuals [5]. Inhibitors of the enzymes, α - glucosidase and α -amylase are recognized as novel anti diabetic drugs. α -glucosidase is the key enzyme which is responsible for the hydrolysis of oligo- and/or disaccharides to simplest sugars absorbable by the body. Inhibition of this enzyme leads to prevention of conversion of disaccharides to monosaccharides, decreasing the absorption of monosaccharides through mucosal border of small intestine [6]. Some of the currently used α -glucosidase and α -amylase inhibitors are acarbose, miglitol and voglibose etc. However, many of these synthetic hypoglycemic agents have their own limitations, which are non-specific, produce serious side effects viz., bloating, abdominal discomfort, diarrhea and flatulence leading to diabetic complications [7]. Recently, herbal medicines are gaining more importance in the treatment of obesity and diabetes as they are free from side effects, easily available and less expensive when compared to synthetic drugs.

The açai palm (Euterpe oleracea of family Arecaceae) is a native tree from the Amazon region, northern South America. Acai berry is used as antioxidant, antidiabetic agent, activate detoxifying enzymes, prevent cancer cell proliferation and anti-inflammatory agent [8]. The mechanism of action behind its use in the treatment of diabetes is not reported. Hence, the present study was



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Vemuri Jyothi,

Department of Pharmacognosy, Sarojini Naidu Vanita Pharmacy Mahavidyalaya, Vijaypuri Colony, Tarnaka, Hyderabad, Telangana, India

Madhuri Pullemla.

Department of Pharmacognosy, Sarojini Naidu Vanita Pharmacy Mahavidyalaya, Vijaypuri Colony, Tarnaka, Hyderabad, Telangana, India

Shaik Nafiroona,

Department of Pharmacognosy, Sarojini Naidu Vanita Pharmacy Mahavidyalaya, Vijaypuri Colony, Tarnaka, Hyderabad, Telangana, India

Geethika Pujari

Department of Pharmacognosy, Sarojini Naidu Vanita Pharmacy Mahavidyalaya, Vijaypuri Colony, Tarnaka, Hyderabad, Telangana, India

Revathi Purama

Department of Pharmacognosy, Sarojini Naidu Vanita Pharmacy Mahavidyalaya, Vijaypuri Colony, Tarnaka, Hyderabad, Telangana, India

Corresponding Author: Vemuri Jyothi,

Department of Pharmacognosy, Sarojini Naidu Vanita Pharmacy Mahavidyalaya, Vijaypuri Colony, Tarnaka, Hyderabad, Telangana, India

Formulation and evaluation of curcumin emulgel for topical delivery

Vemuri Jyothi, Madhuri Pullemla, Shaik Nafiroona, Geethika Pujari and Revathi Purama

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Abstract

Topical drug delivery system is the application of the formulation onto the skin directly treat skin diseases. The gel formulation has a disadvantage to delivery hydrophobic drugs. This can be overcome by formulating novel drug delivery known as Emulgel. Emulgel combines two formulation gel and emulsion. The Emulgel is used to treat skin infections like fungal infections, acne, and psoriasis. The emulgel was formulated and characterised for FTIR studies, pH analysis, spredability, swelling index, drug content, globules size, *in-vitro* drug release, comparative *in-vitro* drug release studies, SEM studies and *in-vitro* drug release kinetics using zero order, first order, highchair model and korsmeyer papas model. FTIR studies provided no evidence of chemical interaction between curcumene and excipients used. The pH of the formulations was within an appropriate range for skin. The swelling index and spredability were optimum for the better patient compliance.

Keywords: emulgel, hydrophobic, emulsion, gel, topical

Introduction

Topical drug delivery system can be defined as system in which API containing formulation is directly applied to skin to treat local cutaneous manifestations ^[1,2]. When other routes of administration like parenteral, sublingual and rectal fails or mainly to treat local skin infections like Tine capitals, Tine padi (fungal infections).

One of the major advantages of topical drug delivery system is to avoid presystolic metabolism, patient inconvenience, and risk by intravenous therapy and different conditions of absorption like presence of enzymes, change in PH [3-5]. Topical medicinal products are diverse in their formulation which are directly applied to the skin and available in liquid to powder consistency, but semisolid preparation is most popular among those formulations. When compare to creams and ointments, gels provide faster drug release but major limitation is unable to deliver hydrophobic drugs. So, to overcome this limitation emulgel is formulated. The routes for topical drug administration can be through ophthalmic, rectal, vaginal and skin as topical routes. Emulex possesses the properties such as thixotropic, greaseless, easily spreadable, and bio-friendly and increases patient acceptability. [6]

Turmeric (Curcuma longa) is widely used popular Indian medicinal plant and belongs to the family of Zingiberaceae. Cur cumin is polyphenolics compound and lipophilic in nature. This active constituent of turmeric is isolated from curcuma longa and it provides colour to turmeric. Traditionally curcumene is being used for its various medicinal properties and exhibits anti-inflammatory, anti-oxidant, anti-bacterial and anticancer activities. The yellow colour of the turmeric is due to the curcumene compound known as diferuloylmethane

The oral administration (up to 8 g per day), it is poorly absorbed, and only the traces of compound appear in blood. It undergoes extensive first-pass metabolism, and hence is a suitable candidate for topical gel formulation. ^[6-10]

II. Materials and methods

Chemicals – Cur cumin was obtained from Yucca Enterprises, Mumbai. HPMC, span 80, tween 80, liquid paraffin, Potassium Dihydrogen Phthalate and Sodium Hydroxide were procured from SD Fine Chemicals Ltd.

Methods

Standard Calibration Curve of Cur cumin

The stock solution (1 mg/ml) was prepared by weighed accurately 10 mg of curcumin emulgel and transferred to a 50 ml volumetric flask then makeup the final volume with methanol.

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FORMULATION AND EVALUATION OF ORAL THIN FILM OF PROCHLORPERAZINE

Mamatha T., Syeda Juveria Fatima and Sri Lalitha G

Department of Pharmaceutics, Sarojini Naidu Vanita Pharmacy Maha Vidyalaya, Tarnaka, Secunderabd. Telangana State, India -500017

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ABSTRACT

The main objective of the present study was to prepare and evaluate the instant release oral thin films of Prochlorperazine, in order to enhance the bioavailability of the drug and to provide rapid onset of action thereby improving patient compliance. The instant release oral thin films of Prochlorperazine were prepared by solvent casting method using film forming polymer like Hydroxypropyl Methylcellulose E-15. The film was evaluated for various physicochemical parameters that include thickness, weight variation, folding endurance, tensile strength, drug content and in vitro drug release studies. No differences were observed in in vitro dissolution of drug from the formulated film F1-F9 as the film instantly gets wet by dissolution medium. The drug release for F3 formulations was about 97.8%. The accelerated stability studies for the optimized film formulations F3 were performed that indicates that the formulated instant release oral thin films were unaffected after initial and 3 months storage under accelerated conditions.

Fast dissolving oral films (FDOFs) or Oral wafers or Oral

strips (OS) or sublingual strips or oral thin films (OTF) are the

most advanced form of oral solid dosage form due to more

flexibility and comfort. It improves the efficacy of APIs by

dissolving within a minute in the oral cavity after the contact

with saliva without chewing and no need of water for the

administration. It gives quick absorption and instant

bioavailability of drugs due to high blood flow and

permeability of oral mucosa is 4-1000 times greater than that

of skin^[5]. OTFs also have an established shelf life of 2-3 years,

depending on the API but are extremely sensitive to

environmental moisture^[6]. The OTFs place as an alternative in

the market due to the consumer's preference for a fast-

dissolving product over conventional tablets / capsules^[7]. The

oral thin-film technology is still in the beginning stages and

has a bright future ahead because it fulfills all the need of

patients. Eventually, film formulations having drug/s will be

commercially launched using the OTF technology^[8]. Oral thin

films, a new drug delivery system for the oral delivery of the

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INTRODUCTION

Oral thin film is a dosage form containing medicinal substances which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue"[1]. About 60% of all dosage forms available are the oral solid dosage form. The lower bioavailability, long onset time and dysphagia patients' turn the manufacturer to the parenterals and liquid orals. But the liquid orals (syrup, suspension, emulsion etc.) has the problem of accurate dosing mainly and parenteral are painful drug delivery, so most patient incompliance. Each pharmaceutical company wants to formulate the novel oral dosage form which has the highest bioavailability, quick action and most patient compliance. So they formulate the fast dissolving tablets by using super disintegrants and hydrophilic ingredients. Fast dissolving drug delivery systems were first developed in the late 1970s as an alternative to conventional dosage forms for Pediatric and Geriatric patients who experience difficulties in swallowing traditional oral soliddosage forms^[2-3]. The main mechanism for the absorption of the drug into oral mucosa is via passive diffusion into the lipoidal membrane^[4].

Sublingual products have been developed for numerous indications ranging from migraines (for which rapid onset of action is important) to mental illness (for which patient compliance is important for treating chronic indications such

drugs, were developed based on the technology of the transdermal patch. The delivery system consists of a very thin oral strip, which is simply placed on the patient's tongue, or any oral mucosal tissue, instantly wet by saliva the film rapidly hydrates and adheres onto the site of application. It then rapidly disintegrates and dissolves to release the medication for oral mucosal absorption or with formula modifications. will maintain the quick-dissolving aspects allow as depression and schizophrenia)^[5]. gastrointestinal absorption to be achieved when swallowed. In contrast to other existing, rapid dissolving dosage forms, *Corresponding author: Mamatha T which consist of lyophilizates, the rapid films can be produced JETIR.ORG

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A REVIEW ON VITAMIN C

Sheetal jadur *1, Sreekanth M², Vamshi Goura³, Pravallika Muthyala ⁴, Akhila G⁵, JVC Sharma⁶

Joginpally B.R Pharmacy College (Jawaharlal Nehru Technological University Hyderabad), Hyderabad, Telangana, India.

Corresponding author Email: sheetal.jadur27@gmail.com Tel: +91 8522955117

ABSTRACT-

Nutrient C inadequacy is regularly because of an absence of day by day sum. Scurvy is portrayed by the event of weakness, myalgia, arthralgia, purpura, draining problems, and later by dental indications. Organic signs are vague: frailty, hypocholesterolaemia, hyperalbuminemia. Clinical doubt is affirmed by the decline in ascorbic corrosive level (< 2 mg/L). It should be deciphered considering the intense stage reactants. The treatment is the organization of 1 g of nutrient C each day for 15 days. Nutrient C exhaustion (ascorbic corrosive: 2 to 5 mg/L) could initiate long haul confusions. The suggested dVitamin C is a water solvent nutrient which is predominantly new products of the soil dietary remittance of nutrient C shield from these dangers.

INDEX TERMS- Vitamin c, scurvy, ascorbic acid, Nutrient c.

I. INTRODUCTION-

Nutrient C is a fundamental supplement which can't be orchestrated by people because of loss of a vital chemical in the biosynthetic pathway [1]. Serious nutrient C inadequacy brings about the possibly lethal infection scurvy . Scurvy is described by debilitating of collagenous constructions, bringing about helpless injury recuperating, and hindered resistance. People with scurvy are profoundly vulnerable to possibly lethal contaminations, for example, pneumonia . Thus, contaminations can fundamentally affect on nutrient C levels because of improved aggravation and metabolic prerequisites. Right off the bat, it was noticed that scurvy frequently followed irresistible pandemics in populaces , and instances of scurvy have been accounted for following respiratory disease . This is especially clear for people who are as of now malnourished.

Nutrient C is likewise a cofactor for the hydroxylase chemicals associated with the combination of catecholamine chemicals, e.g., norepinephrine, and amidated peptide chemicals e.g., vasopressin, which are integral to the cardiovascular reaction to extreme contamination [2]. Besides, research in the course of recent years or so plays uncovered n

At times called ascorbic corrosive, it upholds your invulnerable framework and helps your body utilize the iron you get from food. Your body likewise utilizes it to make collagen, a springy kind of connective tissue that makes up pieces of your body and mends wounds. Also it's a cancer prevention agent that shields your cells from harm. Men need 90 milligrams each day, and ladies need 75 milligrams.

parts for nutrient C in the guideline of quality record and cell flagging pathways through guideline of record factor action and epigenetic marks[3]. For instance, the asparagyl and prolyl hydroxylases needed for the down regulation of the pleiotropic record factor hypoxia-inducible variable 1α (HIF1 α) use nutrient C as a cofactor [4]. Late



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A Review: Poly Herbal Lozenges For Cold And Flu

Akhila G*1, Sreekanth M*2, Sheethal J 3, Vamshi G4, Dr JVC sharma5. Joginpally B. R pharmacy college (Jawaharlal Nehru Technology University Hyderabad), Hyderabad, Telangana, India.

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ABSTRACT :Lozenges are solid dosage form which are intended to slowly dissolve in the mouth for therapeutic effect. A small usually sweetened and flavored medicated material that is designed to be held in the mouth. Common cold and flu are common disease which usually infect the system include symptoms respiratory headache, fever, runny nose and cough. It is a small, typically medicated tablet intended to dissolved slowly in the mouth temporarily stop cold and coughs. Both cold and cough respiratory illnesses, but they are caused by different viruses only, including rhinoviruses, seasonal corona viruses.

Key words: polyberbal lozenges, common col, flu polyberbal, lozenges, formulations, cold, flu, standardization.

I. INTRODUCTION:

The lozenges are intended to be dissolved or disintegrated slowly in the mouth. They contain one or more active ingredients and are flavored and sweetened so as to be pleasant tasting. Lozenges is a solid preparation consisting of sugar and gum the later giving strength and cohesiveness to the lozenges facilitating slow release of the medicaments.

HISTORY OF LOZENGES

Lozenges originated ancient , specifically 1000BC. Then , they were often made of honey with flavors ranging from citrus to spice .

In the 19th century, however, lozenges took on a far less simple formula when doctors began adding morphine and heroine to tablets in an effort to stop

the cough or cold before it happens. Cough drops was first advertised in the year 1850 and ludens created in 1880.

About the disease

A common viral infection of the nose and throat.

IN contrast to the flu, a common cold can be caused by many different types of viruses. The condition is generally harmless and symptoms usually resolves within two weeks. Flu symptoms are similar, but include fever, headache and muscles soreness. Cold symptoms are runny nose, congestion, and cough.

Cold: the common cold is one of most frequent human illnesses and is responsible for substantial morbidity and economic loss. No consistently effective therapy for the common cold has been well documented, but evidence suggests that several possible mechanisms may make polyherbal an effective treatment.

Flu: a common viral infection that can be deadly, especially in high-risk groups

The flu attacks the lungs, nose and throat. Young children, older adults, pregnant women and people with chronic disease or weak immune systems are at high risk. And spreads easily.

About herbal drugs

An herb is a plant or plant part used for its scent, flavor, or therapeutic properties. Herbal medicines are one type of dietary supplement.

They are solid as tablets, capsules, powders ,teas, extracts, and fresh or dried plants. And it will improve health.

Review Article



A Review: Zika Virus

Pravalika Muthyala*, Sreekanth M, Sheetal Jadur, Vamshi Goura, Akhila Gangi

Joginpally B.R Pharmacy College (Jawaharlal Nehru Technological University Hyderabad), Hyderabad, Telangana, India.

*Corresponding author's E-mail: Muthyalapravalika1424@gmail.com

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ABSTRACT

Zika virus (ZIKV) is a newly emergent relative of the Flaviviridae family and to linked to dengue and chikungunya. ZIKV is one of the rising pathogens promptly surpassing geographical borders. ZIKV infection was characterized by mild disease with fever, headache, rash, arthralgia, and conjunctivitis with exceptional reports of an association with Guillain -Barre syndrome (GBS) and microcephaly. However, Since the end of 2015, an increase in the number of GBS associated cases and an astonishing amount of microcephaly in foetus and new-borns in Brazil have been related to ZIKV infection, raising serious worldwide public health concerns. ZIKV is transmitted by the bite of infected female mosquitoes of Aedes species. Clarifying such worrisome relationships is thus, a current unavoidable goal. Here, we extensively described the current understanding of the effects of ZKIV on heath, clinical manifestation, diagnosis and treatment options based on modern, alternative and complementary medicines regarding the disease.

Keywords: Zika virus, Flaviviridae, Neurological infections, fetal development, Microcephaly.

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INTRODUCTION

ika fever (also called Zika virus disease) is associate degree unwellness caused by the Zika virus. Most cases don't have any symptoms. Symptoms typically last but seven days "zika virus: Rapid spread in the new world." Symptoms may include fever, joint pain, red eyes, headache, and a maculopapular rash. Infection has joined to Guillain barre syndrome (GBS).

Zika fever is principally unfold via the bite of mosquitoes of the arthropod genus kind. It can even be probably unfold by sex and blood transfusions. The disease may spread from mother-to-child within the womb and cause microcephaly. Diagnosis is by testing the blood, urine, or saliva for the virus's RNA when the person is sick. Interference involves decreasing mosquitoes bites in areas wherever the illness happens efforts embody the utilization of repellent, covering abundant of the body with consumer goods, dipteran nets, and obtaining eliminate standing water wherever mosquito reproduce there's no effective immunizing agent. Health officers counselled that ladies in area plagued by outbreaks think which pregnant lady not travel areas wherever outbreaks were occurring whereas there is nospecific treatment paracetamol (acetomenophen) could facilitate with the symptoms admission to hospital never necessary.1



Figure 1: Aedes aegypti

Signs and symptoms

The most common signs and symptoms of Zika fever are fever, rash eyes, conjunctivitis (red eyes) muscle and joint pain, and headache, which are similar to signs and symptoms of dengue and chicken gunya fever. The time from a mosquito bite to developing symptoms not yet known, but is probably a few days to a week, the disease lasts for several days to a week and is usually mild enough that people do not have to go a hospital.⁴

Gullain bare syndrome

Zika virus infections are connected to GBS, that is that fast onset of muscle weakness which will make dysfunction. Whereas each will happen to a similar time, its troublesome to definitely purpose to zika virus because the reason for GBS. Many countries suffering from zika outbreaks have rumored will increase within the rate of GBS and three deaths thanks to zika connected Gullain -barre rumored in Colombia.¹⁵



FORMULATION & EVALUATION OF VORICONAZOLE OINTMENT FOR TOPICAL DELIVERY

Shanthi priya^{1*,} Nirmala Rangu², Rohini Reddy³

ABSTRACT

The present study was undertaken to develop ointment containing voriconazole selectively inhibits 14-alpha-lanosterol demethylation in fungi, preventing the production of ergosterol, an essential constituent of the fungal cell membrane, and resulting in fungal cell lysis. (NCI04). The ointment containing voriconazole was prepared by a fusion method., The specified concentration of polyethylene glycol (PEG) 4000, PEG400 and PEG 600 The amount of voriconazole remains fixed (5 mg) for all the eight formulations whereas the amounts of PEG400 will be used for first four formulations i.e. F-1,F-2,F-3,F-4,and PEG 600 for F-5,F-6,F7 & F-8 formulations respectively. The prepared ointments were evaluated for Physical Examination, Determination of pH, Measurement of viscosity, Spreadability Extrudability Invitro Drug release study. We can conclude that all the parameters were within the acceptable limits.

KEYWORDS:- voriconazole, polyethylene glycols, antifungal activity

1.INTRODUCTION:

The studies were conducted with an object to develop a desired ointment for treatment of fungal infection like eczema itching, purities'. Main objective of this study is to formulate the ointment with different ointment bases having good consistency, diffusion, antifungal and antiseptic properties. To assess the efficacy of formulations assay, spread ability, permeability, drug release, uniformity, viscosity, diffusivity, stability, and other physical characteristics were evaluated. The ointment base was prepared and formulation of ointment was done by incorporating the active ingredients in most effective ratio in the base by fusion method. The PEG ointments were prepared with changing the type of the liquid PEG (low molecular weight). Then, the viscosity and the voriconazole release from the prepared formulations were studied.[1,2]

1.1 Characteristics of an ideal ointment[3,4,5]

- 1. It should be physically and chemically stable.
- 2. The base of ointment should possess no therapeutic action.
- 3. In ointment base, finely divided active ingredient should be uniformly distributed.
- 4. The ointment should be sooth and free from grittiness

1.2 Types Of Ointments Bases

The medicated stuff or the ingredients present inside the ointment is actually the main base of ointments. There are ointment bases:

- 1. Hydrocarbon bases. e.g. hard paraffin and paraffin, microcrystalline wax and ceresine.
- 2. Absorption bases. e.g. wool fat, beeswax.
- 3. Water soluble bases. e.g. PEG 200, 300, 400.
- 4. Emulsifying bases. e.g. Emulsifying wax, Vegetable oils like as coconut oil, sesame oil, olive oil, almond oil and peanut oil [6].

¹Associate Professor, Department of Pharmaceutics, SurabhiDayakarRao College of Pharmacy, Rimmanaguda, Gajwel, Siddipet, Telangana, India.

²Associate Professor, Department of Pharmaceutics, SurabhiDayakarRao College of Pharmacy, Rimmanaguda, Gajwel, Siddipet, Telangana, India.

³Associate Professor, Department of Pharmaceutics, SurabhiDayakarRao College of Pharmacy, Rimmanaguda, Gajwel, Siddipet, Telangana, India.

Original Research Paper



Pharmaceutical Science

FORMULATION AND EVALUATION OF LOSARTAN POTASSIUM IMMEDIATE RELEASE CAPSULES

Shanthi Priya

Department of Pharmaceutics, Surabhi Dayakar Rao College of Pharmacy, Rimmanaguda, Gajwel, Siddipet, Telangana-502312.

Rohini Reddy*

Department of Pharmaceutics, Surabhi Dayakar Rao College of Pharmacy, Rimmanaguda, Gajwel, Siddipet, Telangana-502312. *Corresponding Author

ABSTRACT Hard gelatin capsule contains Losartan potassium granules. Losartan is an angiotensin-receptor blocker it is an antihypertensive drug which is used to treat hypertension.it was designed to achieve immediate release of drug from the dosage form, this was mainly designed to increase therapeutic efficacy and to improve patient compliance. Advantages of hard gelatin capsule are rapid drug release, flexibility of formulation and better bioavailability than tablets. The main aim of this present work is to release the drug immediately from the hard gelatin capsule containing losartan potassium. Losartan potassium granules were prepared by using wet granulation method by different concentrations of sodium starch glycolate and then the air dried granules are filled into empty hard gelatin capsules for the dissolution studies. The prepared granules were evaluated pre compressional and post compressional properties. Stability study shows that there was no significant change in disintegration time, drug content and in-vitro drug release of the formulation. The, formulation F5 was considered as best formulation for immediate release of Losartan potassium.

KEYWORDS: Losartan potassium, sodium starch glycolate, in-vitro drug release

INTRODUCTION:

A hard gelatin capsule is a type of capsule that is usually used to contain medicine in the form of dry powder or very small pellets. The term capsule is derived from the latin word capsula, meaning a small container. Gelatin has the property of disintegrating when comes in contact with the water thereby releasing the medicament completely. The main advantage of hard gelatin capsules rapid drug release is possible, flexibility of the formulation which cant be obtained by tables and selead HGCs are good barriers to atmospheric oxygen. Main disadvantages of hard gelatin capsules are filling the bulky materials is a problem, equipment filling is slower than tableting and more costly than tablets the process may be very simple or complex depending on the characteristics of powders.

Losartan is an angiotensin-receptor blocker (ARB) that may be used alone or with other agents to treat hypertension.it is well absorbed Losartan may be used to treat hypertension, left ventricular hypertrophy and diabetic nephropathy. It may also be used as an alternative agent for the treatment of systolic dysfunction, myocardial infarction, coronary artery disease, and heart failure.

MATERIALS AND METHODS:

Losartan potassium, active pharmaceutical ingredient was procured from Research lab fine chem. Industries. Sodium starch glycolate (Loba Chemie Pvt. Ltd., Mumbai, India), starch (Qualigens Fine Chemicals, Mumbai, India), Magnesium sterate (Prime laboratories, Hyderabad), talc(S.D Fine chemicals, Hyderabad, India were procured and used in this investigation.the entire chemicals of analytical grade and double distilled water used throughout the experiment. ⁶⁻⁹

Formulation and development of emulgel:

Granules were prepared by wet granulation method. losartan potassium, sodium starch glycolate and lactose are weighed and mixed uniformly. Required quantity of starch paste was prepared and added drop wise to the blend. The wet granules prepared were passed through sieve #10 & dried for 15 minutes. The air dried granules are again passed through sieve #22. magnesium stearate & talc were accurately weighed added to the granules. The prepared granules are filled to the Size #3 empty hard gelatin capsule. The composition of formulations has been examined in **Table 1**.

Table 1:composition of formulation

Ingredients (in gms)	F1	F2	F3	F4	F5	F6
Losartan potassium	50	50	50	50	50	50
Sodium starch gylcolate	20	25	29	30	35	38
lactose	16	19	15	14	9	6
Magnesium stearate	4	4	4	4	4	2
talc	2	2	2	2	2	2

Evaluation Parameters

Pre formulation tests

Percentage Yield losartan potassium granules were prepared by using wet granulation method.50mg of granules were weighed and percentage yield was calculated by using the following equation.

Yield=M/MoX100

Where, M = weight of granules and Mo = total expected volume

2. Angle of Repose [6] This was determined by using the funnel method. granules was allowed to flow freely from the funnel at a distance of 2 cm from the tip of the funnel to the horizontal surface to form a heap. The heap of the cone was marked and the pile of granules was also poured off. The average of the two diameters were also determined. The angle of repose was then calculated from the height of the heap (h) and the radius (r) from the relation:

$\alpha = \tan -1 (h/r)$

3. Bulk Density [7] Apparent bulk density (ρb) was calculated by placing presieved drug excipients blend into a graduated measuring cylinder and measuring the volume (Vb) and weight (M)

$\rho \mathbf{b} = \mathbf{M}/\mathbf{V}\mathbf{b}$

4. Tapped Density [8] The measuring cylinder containing a known mass of powder blend was tapped for a fixed number of taps. The minimum volume (Vt) occupied in the cylinder and the weight (M) of the blend was measured. The tapped density (ρt) was calculated using following formula:

$\rho t = M/Vt$

5. Hausner's Ratio [9] It indicates the flow properties of the powder. It is usually determined from the ratio between the tapped density (TD) and the bulk density (BD).

Hausner's ratio = ρt\ρb

Where, $\rho t =$ Tapped density and $\rho b =$ Untapped bulk density

6. Carr's Index [9] The simplest way of measurement of free flow property of powder is compressibility, an indication of the ease with which a material can be induced to flow is given by % compressibility which is calculated as follows:

$C = (\rho t - \rho b) / \rho t * 100$

Where, $\rho t = \text{Tapped density and } \rho b = \text{Untapped bulk}$

Evaluation of losartan potassium capsules:.

1. Disintegration Time [10] Disintegration test on capsules were carried out using a disintegrating apparatus (Type: ZT3/1, Erweka mbH, Heusenstamn, Germany) at 37 \pm 2 °C. The disintegration medium used was distilled water. A disk was placed on each capsule to prevent it from floating. The time taken for all six capsules to disintegrate leaving only remnants of gelatin shell on the mesh was recorded.

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ANALYTICAL METHOD DEVELOPMENT AND VALIDATION OF FLUCONAZOLE AND TINIDAZOLE IN BULK AND TABLET DOSAGE FORM BY RP-HPLC

DANDAMUDI SP 1 , BOGGULA N 1 , SAYEED M 1 , SHIMMULA RR 2 , CHINTHALA SP 2 AND MANDHADI JR *3

- 1: School of Pharmacy, Anurag University, Venkatapur, Ghatkesar, Hyderabad, Telangana, India
- 2: Surabhi Dayakar Rao College of Pharmacy, Rimmanaguda, Gajwel, Siddipet, Telangana, India
 - **3:** Faculty of Pharmaceutical Sciences, Assam Down Town University (AdtU), Panikhaiti, Guwahati, Assam, India

*Corresponding Author: Dr. Jithendar Reddy Mandhadi: E Mail: jithendar m@hotmail.com

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ABSTRACT

An analytical method consists of a detailed, stepwise list of instructions to be followed in the qualitative, quantitative or structural analysis of a sample for one or more analytes and using a specified technique. A facile and rapid isocratic reverse phase high performance liquid chromatography assay method has been developed for simultaneous estimation of fluconazole and tinidazole in bulk and tablet. A waters HPLC system with Empower software was used. Inertsil ODS Column with phosphate buffer of pH 3.0 and methanol in the ratio of (70:30 v/v) as mobile phase at flow rate of 1 ml/min was employed for the analysis. The column was maintained at ambient temperature (27 °C). The eluent was monitored using PDA detector at 210nm. The run time was found to be 8 min. The developed method was validated as per ICH (International Conference on Harmonisation) guidelines. The developed method was found to be linear over a workable drug concentration, accurate, precise and robust. This fast and inexpensive method is suitable for research laboratories as well as for quality control analysis in pharmaceutical industries.

Keywords: RP-HPLC, isocratic, validation, fluconazole, tinidazole, precision

Formulation and Evaluation of Sustained Release Tablets of Losartan Potassium

Rohini Reddy¹, Dr M Venkata Ramana², Ch.Shanthi Priya³, M.Praveen⁴, K.Srikanth⁵, G.Srinivas⁶, CH.Vaishnavi⁷, G.Suchitha⁸

¹Associate Professor, Department of Pharmaceutics, SurabhiDayakarRao College of Pharmacy, Rimmanaguda, Gajwel, Siddipet, Telangana, India.

²Principal, Department of Pharmaceutics, SurabhiDayakarRao College of Pharmacy, Rimmanaguda, Gajwel, Siddipet, Telangana, India.

³Associate Professor, Department of Pharmaceutics, SurabhiDayakarRao College of Pharmacy, Rimmanaguda, Gajwel, Siddipet, Telangana, India.

⁴Student, Department of Pharmaceutics, SurabhiDayakarRao College of Pharmacy, Rimmanaguda, Gajwel, Siddipet, Telangana, India.

⁵Student, Department of Pharmaceutics, SurabhiDayakarRao College of Pharmacy, Rimmanaguda, Gajwel, Siddipet, Telangana, India.

⁶Student, Department of Pharmaceutics, SurabhiDayakarRao College of Pharmacy, Rimmanaguda, Gajwel, Siddipet, Telangana, India.

⁷Student, Department of Pharmaceutics, SurabhiDayakarRao College of Pharmacy, Rimmanaguda, Gajwel, Siddipet, Telangana, India.

⁸Student, Department of Pharmaceutics<mark>, SurabhiDaya</mark>karRao College of Pharmacy, Rimmanaguda, Gajwel, Siddipet, Telangana, India.

ABSTRACT:

The present study was undertaken to develop sustained release (SR) tablets of Losartan potassium, an angiotensin-II antagonist for the treatment of hypertension. The tablets were prepared by wet granulation method, with ethyl cellulose. The amount of Losartan potassium remains fixed (100 mg) for all the six formulations whereas the amounts of ethyl cellulose were 50mg,60mg,70mg,80mg,90mg and 100mg for F-1, F-2, F-3, F-4, F-5 F-6 & F7 formulations respectively. The evaluation involves three stages: the micromeritic properties evaluation of granules, physical property studies of tablets, and in-vitro release kinetics studies. The USP apparatus type II was selected to perform the dissolution test, and the dissolution medium was 900 mL phosphate buffer pH 6.8. The test was carried out at 75 rpm, and the temperature was maintained at 37° C \pm 0.5°C.

KEYWORDS:- Losartan potassium, Sustained release, ethyl cellulose, in-vitro drug release and anti-hypertensive drug

1. INTRODUCTION:

The objective of an ideal drug delivery system is to deliver adequate amount of drug for an extended period for its optimum therapeutic activity. Most drugs are inherently not long-lasting in the body, and require multiple daily dosing to achieve the desired blood concentration to produce therapeutic activity. To overcome such problems greater attention has been focused on sustained release drug delivery system[1].

Losartan is an angiotensin-receptor blocker (ARB) that may be used alone or with other agents to treat hypertension. It is well absorbed Losartan may be used to treat hypertension, left ventricular hypertrophy and diabetic nephropathy. It may also be used as an alternative agent for the treatment of systolic dysfunction, myocardial infarction, coronary artery disease, and heart failure. The objective of the present investigation were to prepare sustained release tablets of Losartan Potassium by using ethyl cellulose at six different concentrations, and to compare the in-vitro characteristics (weight variation, thickness and diameter, hardness, friability, drug content,) of the developed tablets [2].

2. MATERIALS AND METHODS:

Losartan potassium, active pharmaceutical ingredient was procured from Research lab fine chem. Industries. Ethyl cellulose (Loba Chemie Pvt. Ltd., Mumbai, India), starch (Qualigens Fine Chemicals, Mumbai, India), Magnesium sterate (Prime laboratories, Hyderabad), talc(S.D Fine chemicals, Hyderabad, India were procured and used in this investigation [3].

Formulation & Evaluation of Ciprofloxacin Controlled Release Floating Capsules

Ch. Shanthi priya¹, Dr M Venkata Ramana², Dr Rangu Nirmala³, Samreen begum⁴, R.Vijay⁵, Bhavana⁶, A.Sandhya⁷, Samreen⁸

¹Associate Professor, Department of Pharmaceutics, SurabhiDayakarRao College of Pharmacy, Rimmanaguda, Gajwel, Siddipet, Telangana, India.

²Principal, Department of Pharmaceutics, SurabhiDayakarRao College of Pharmacy, Rimmanaguda, Gajwel, Siddipet, Telangana, India.

³Associate Professor, Department of Pharmaceutics, SurabhiDayakarRao College of Pharmacy, Rimmanaguda, Gajwel, Siddipet, Telangana, India.

⁴Student, Department of Pharmaceutics, SurabhiDayakarRao College of Pharmacy, Rimmanaguda, Gajwel, Siddipet, Telangana, India.

⁵Student, Department of Pharmaceutics, SurabhiDayakarRao College of Pharmacy, Rimmanaguda, Gajwel, Siddipet, Telangana, India.

⁶Student, Department of Pharmaceutics, SurabhiDayakarRao College of Pharmacy, Rimmanaguda, Gajwel, Siddipet, Telangana, India.

⁷Student, Department of Pharmaceutics<mark>, SurabhiDaya</mark>karRao College of Pharmacy, Rimmanaguda, Gajwel, Siddipet, Telangana, India.

⁸Student, Department of Pharmaceutics, <mark>SurabhiD</mark>ayak<mark>ar</mark>Rao College of Pharmacy, Rimmanaguda, Gajwel, Siddipet, Telangana, India.

ABSTRACT

Capsules are solid preparations in which the drug substances and/or excipients are enclosed in either a soft or hard soluble shell. The shell is normally made of gelatin or suitable polymeric material and results in a simple, tasteless, odourless, elegant, easy to swallow dosage form without the need for a secondary coating step. Controlled release dosage forms have attracted considerable interests as a mean of improving the dissolution rate & hence possibly bioavailability range of hydrophobic drugs. The poor solubility of ciprofloxacin leads to poor dissolution & hence variation in bioavailability. The purpose of present investigation was to formulate and evaluate controlled release floating capsules of ciprofloxacin with improved solubility & dissolution rate. In present study granules using various carriers like mannitol & lactose indifferent ratios were prepared by wet granulation method using polymer such as ethyl cellulose & HPMC. The prepared granules were evaluated to preformulation studies such as angle of repose (18.41-24.22), bulk density, tapped density, compressibility index (11.31-12.75) & hausner's ratio. All the parameters shows that the granules having good flow properties. These granules had converted into the capsule forms. Then the formulated capsules were taken to the evaluation studies such as weight variation, release study, buoyancy & floating duration (more than 6 hrs.). We can conclude that all the parameters were within the acceptable limits.

Keywords:- Controlled release, floating, capsules, Ciprofloxacin, buoyancy

1. Introduction

Oral ingestion is the most convenient & commonly employed route of drug delivery due to its ease of administration, high patient compliance, cost effectiveness, least sterility constraints & flexibility in the design of dosage form. It was used to enhance the solubility of poorly soluble drugs [1,2]. Low aqueous solubility is the major problem encountered with formulation development of new chemical entities as well as generic development. The poor solubility & low dissolution rate of poorly water soluble drugs in the aqueous gastrointestinal fluids often cause insufficient bioavailability. Especially for class II (low solubility & high permeability) substances according to the BCS, the bioavailability may be enhanced by increasing the solubility & dissolution rate of the drug in the gastrointestinal fluids. As for BCS class II drugs rate limiting step is drug release from the dosage form & solubility in the gastric fluids & not the absorption, so increasing the solubility in turn increases the bioavailability for BCS class II drugs [3,4]. Adrug with poor bioavailability is the one with



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Review Article

SPHERICAL CRYSTALLIZATION: A TOOL TO IMPROVE SOLUBILITY OF DRUGS

Hema Latha B*, Manisha E, Harshavardhini G, Hyma P

Department of Pharmaceutics, Sarojini Naidu Vanita Pharmacy Maha Vidyalaya, Osmania University,
Tarnaka, Hyderabad, Telangana, India
**Corresponding author: hema81731@gmail.com

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ABSTRACT

Spherical crystallization is a technique in which crystallization and agglomeration are carried out synchronously in one step to form compact spherical form. The most common methods used in spherical agglomeration are quasi emulsion solvent diffusion method, ammonia diffusion system, neutralization technique and co-agglomeration. It succeeded to improve dissolution property of poorly soluble drugs. This can change drug powder properties such as flowability, wettability, packability, compressibility. It has wider applications in improvement of poorly compressible drugs; it has wider application in improvement of compressability of poorly compressible drugs, masking bitter taste of drugs, improving dissolution property, bioavailability and solubility of drugs. Agglomeration crystals converted into tablet forms thus helping us by saving time and reducing cost.

Keywords: Bioavailability, Agglomeration, Quasi Emulsion, Flowability, Compressible.

1. INTRODUCTION

Solid dosage forms such as tablets and capsules are used due to special features like unit dosage form with great dose precision, least content variability, lower cost and easy administration by patient. Direct compression is a simple and economical technique and solutions for manufacture of tablets [1]. Direct compression of drugs needs good micrometric properties of drug particles, such as shape and size, flow ability and honest reproducible compressibility are of crucial importance for formulation of highly solid dosage forms. Poor solubility of drugs depends on particle size which is always an issue due to its impact on dissolution properties. Micronized drug particles have a large specific area and provide a way to improve the dissolution rate [2]. Especially, the flow ability of crystals is very poor so these crystals are difficult to handle. During manufacturing, the bioavailability of drug can be enhanced by increasing solubility of bulk drug powder. Different novel methods are developing to increase the bioavailability of drugs that naturally have poor aqueous solubility; it is a great challenge to solid dosage form formulators [3]. Mechanical micronization of sparkling (crystalline) drugs and adding of surfactants during the process of crystallization are commonly used techniques to improve the bioavailability of poorly soluble drugs. Crystallization and agglomeration can be carried out at the same time in single step by spherical crystallization which is a particle design technique. Adding of surfactant normally led to slight increase in aqueous solubility to overcome this tissue. Kawashima developed a spherical crystallization technique. He used spherical crystallization technique in 1986 for size development of drugs in field of pharmacy. He determined the spherical crystallization as "The process of agglomeration that change crystalline drugs straight into a compacted spherical form.

Spherical agglomerates are prepared to Increase the flowability, compressibility, bioavailability of drugs and to mask the bitter taste of drugs [4].

Spherical crystallization utilizes three solvents: good solvent (dissolution medium for drugs); bridging liquid (drugs having wetting property dissolved by this medium) and bad solvent (drug substance immiscible the solvent) [5]. Spherical crystallization can be achieved by several methods such as simple spherical crystallization, emulsion solvent diffusion, ammonia diffusion and neutralization. The process of spherical crystallization principle involved in flocculation zone, zero growth zone, fast growth zone, and constant size zone [6].



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Research Article

FORMULATION AND EVALUATION OF ORODISPERSIBLE TABLETS OF ACECLOFENAC BY DIRECT COMPRESSION METHOD

Hyma Ponnaganti*, Kaveri Anke

Department of Pharmaceutics, Sarojini Naidu Vanita Pharmacy Mahavidyalaya, Hyderabad, Telangana, India *Corresponding author: rk_hyma@yahoo.com

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ABSTRACT

Nowadays, Oro dispersible tablets are gaining much importance because it is easily approachable and due to its patient compliance. In this study, Formulation and evaluation of one such tablets of Aceclofenac by direct compression method using super disintegrants like Cross carmellose sodium (CCS) was performed.

Due to low water soluble property of aceclofenac, it has poor dissolution and bioavailability. In order to minimize this property OTD's are prepared. ODT's were prepared by direct compression method using super disintegrant i.e Cross Carmellose Sodium (CCS) in different concentrations. The prepared powder blend was subjected to various evaluation studies like pre compression parameters like angle of repose, tapped density, and bulk density. Post compression parameters like weight variation, hardness, friability, drug content, wetting time, disintegration and dissolution studies were performed. The drug excipients compatibility was verified by FTIR.

The precompression evaluation studies showed that the prepared powder blend has good flow property. The hardness and friability revealed that it has good mechanical strength with acceptable disintegration time. The optimized formulation indicated good *in vitro* drug dissolution profile with maximum drug being released at all the time intervals indicates an ideal profile for the development of ODT's. The results of pre compression studies and post compression along with FTIR are presented.

Keywords: Oro dispersible tablets, Aceclofenac, FTIR, Super disintegrant, Cross carmellose sodium.

1. INTRODUCTION

Novel drug delivery system (NDDS) aims to improve safety and efficacy of drug molecule by formulating a convenient dosage form for administration and to achieve better patient compliance; one such approach is orodispersible tablets [1]. Oral medication delivery methods, particularly tablets, are the most frequently used dosage forms because they are small, provide a consistent dose, and are painless to administer [2]. Dysphagia is more common in the elderly and children due to physiological abnormalities associated with both populations. Dysphagia affects approximately one-third of the population and is linked to a variety of diseases such as parkinsonism, diabetes mellitus (DM) [3], mental impairments, motion sickness, unconsciousness, and lack of water [4,5]. Because of benefits in dosage, stability, storage, cost, and transportation, the World Health Organization (WHO) now advises that dispersible tablets be preferred over suspensions wherever available. Patient compliance may be enhanced using dispersible tablets and Orally Disintegrating Tablets (ODTs), especially in juvenile, geriatric, and institutionalised patients [6].

Orodispersible tablets (ORDs), sometimes known as "mouth dissolving tablets," are solid dosage forms that dissolve rapidly in the oral cavity in less than 1 minute [7] and combine the benefits of both liquid and traditional tablet formulations, making it easier to consume the medicine in a liquid dose form. ORDs breakdown quickly in the mouth with the assistance of saliva [8] to create dispersion that may be readily ingested without the need for water [9]. Other benefits of ODTs that have been studied include their capacity to improve the bioavailability of medicines that are poorly water soluble by improving dissolution profiles [10].

An ideal ODT has a pleasing mouth feel, sufficient hardness, and an appropriate friability limit, and is manufactured using traditional methods [11].

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Tetralogy of Fallot - A Case Report

Atufa Tahur¹, Omera Begum², Dr. Sujala Aakaram³

¹Pharm.D (Intern), Sarojini Naidu Vanita Pharmacy Maha Vidyalaya, Secunderabad, Mareedpally, Telangana 500017, India

²Pharm.D (Intern), Sarojini Naidu Vanita Pharmacy Maha Vidyalaya, Secunderabad, Mareedpally, Telangana 500017, India

³Assistant Professor, Sarojini Naidu Vanita Pharmacy Maha Vidyalaya, Secunderabad, Mareedpally, Telangana 500017, India

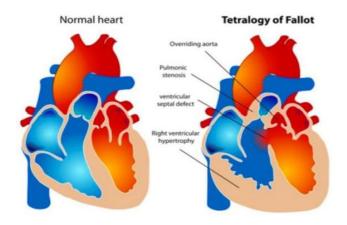
Corresponding Author Email: atufatahur1234[at]gmail.com

Abstract: TOF is a cardiac abnormality consisting of a tetrad of heart defects (Ventricular Septal Defect, Pulmonary Stenosis, Overriding Aorta and Right Ventricular Hypertrophy). Various diagnostic test to confirm TOF includes chest x-ray, echocardiogram, ECG, pulse oximetry test, MRI, Cardiac catheterization. In this case the patient was reported with complains of sudden onset of shortness of breath (SOB) along with sweating since 1 year. The confirmatory test of TOF in this patient was ECG, 2D echo, CT-coronary angio. Post confirmation of TOF, the patient underwent an uneventful ICR (Intra Cardiac Repair) surgery and hence the overall QoL of patient has been improved.

Keywords: TOF, ICR, tetrad of heart defects, shortness of breath, sweating.

1. Introduction

Tetralogy of fallot is a cyanotic congenital heart disease, comprises of four different heart defects as, ventricular septal defect (VSD), right ventricular outflow tract (RVOT) obstruction, overriding aorta and right ventricular hypertrophy.^[1]



- **Ventricular septal defect** is a defect or hole in the septum which separates the ventricles of the heart. A septum is a barrier that prevents the mixing of blood from both the sides of ventricles. [2]
- **Right ventricular outflow tract obstruction** is the narrowing of the pulmonary valve which obstructs the blood outflow from the right ventricles to the lungs (pulmonary stenosis).
- Overriding aorta in TOF, the aorta is displaced and found between the left and right ventricle. Which causes deoxygenated blood to flow into the aorta instead of the pulmonary artery^[3]
- **Right ventricular hypertrophy** is the thickening of the muscular walls of the right ventricle, which occurs because the right ventricle is pumping at high pressure and can contribute to obstruction of blood flow through the pulmonary valve. [2]

TOF has prevalence of 3 cases per 10,000 live births as estimated world-wide. Regardless of its low prevalence, it is the most frequently occurring congenital heart defect (CHD).TOF illustrates 5-10% of all CHD in the general population of 0.8% of global birth prevalence. [4]

2. Signs and Symptoms

Severity of TOF symptoms varies and depends on degree of blood flow obstruction and includes:

- cyanosis (bluish coloration of skin due to low oxyhaemoglobin levels)
- shortness of breath (mainly during eating or exercise)
- fainting
- fatigue
- heart murmur
- failure to gain weight
- irritability
- clubbing
- squatting
- prolonged crying in infants

Tet spell- caused by rapid decrease in the levels of oxygen in blood and commonly seen in young infants (2 to 4 months old). [5]

3. Causes and Risk Factors

The exact etiology of TOF is still not known. However, around 15% of people have a specific genetic abnormality, either due to defective gene or chromosome, and it can be inherited [6] Other possible reasons that may arise during pregnancy include environmental exposure such as:

- Overuse of alcohol
- Viral infections (rubella)
- Phenylketonuria
- Taking seizures medications
- Diabetes
- Late pregnancy (>40 years age)

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Cleaning method development and validation by UV method for quantitative assessment of favipiravir residue in manufacturing area

R. Swetha Sri, S. Pravallika, Guntupally Chakravarthy*, K. Bhavya Sri and M. Sumakanth

Department of Pharmaceutical Analysis, RBVRR Women's College of Pharmacy, Hyderabad-500027, Telangana State, India *College of Pharmacy, KLEF, Vaddeswaram, Guntur-522502, Andhra Pradesh, India

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Abstract

Favipiravir is a potent antiviral substance and has one of the drugs of choice in treating patients affected with COVID-19. A well-prepared cleaning validation master plan was proposed and executed for ensuring the low level of carryover of favipiravir into the next drug product. The current study aimed at developing a precise analytical method using a UV spectrophotometer and validating the same for verification of residues of favipiravir in the manufacturing equipment. A stratified swab sampling method was employed for collecting the residues on a stainless steel 316 sheet $(4 \times 4 \times 2 \text{ mm})$. Swabs were streaked ten times bidirectionally all along the SS plate horizontally, vertically, and diagonally as an approach to collect the residue. UV detection was made at λ max 367 nm using methanol as diluent. The calibration curve was found to be linear in the range of 1 to 10 μ g/ml. With a regression value of $R^2 = 0.999$. Method precision and intermediate precision were carried out and RSD was found to be 0.06 and 0.058%. Accuracy at three different concentrations was performed and found to be 98.8% to 102% in (50,100,150%). %recovery factor was found to be 99.09% (usually it should be >80%). All the validation parameters were performed and they were within the limits. The simplicity of the developed spectrophotometric method can help analyze the favipiravir on a routine basis.

1. Introduction

In the pharmaceutical industry, there is an incredible need for cleaning equipment and handling regions. Inappropriate cleaning can prompt defilement and cross-contamination (Agrawal *et al.*, 2020). A drug product can be tainted by different residue materials like residues of recently utilized dynamic drug fixings, a natural substance, cleaning specialists and residue particles (Baokar *et al.*, 2013). The primary goal of GMP comprises the anticipation of contamination and cross-contamination of materials. The purpose of cleaning validationis to check the adequacy of the cleaning strategies for the evacuation of deposits of the past item, additives, cleaning specialists and microbial pollutants. Cleaning validation satisfies the necessity of administrative bodies and keeps up with item quality and security of the purchasers (Forsyth and Haynes, 1998).

Favipiravir is a type of antiviral drug. Favipiravir was approved in Japan in 2014 to treat cases of influenza during a pandemic condition (Bharti mittu and Chauhan, 2015). It is most typically used to treat patients with COVID-19. 6-fluoro-3-hydroxy-2-pyrazine carboxamide is its biochemical name, and it is sold under the brand names; avigan, fabiflu and favipil. A pyrazine derivative, favipiravir is an antiviral drug (Blessy *et al.*, 2014). The method involves the inhibition of the RNA-dependent RNA polymerase molecule, which is required for viral genome transcription and replication. Toyama

Corresponding author: Dr. G. Chakravarthy

College of Pharmacy, KLEF, Vaddeswaram, Guntur-522502, Andhra

Pradesh, India

E-mail: chakra_varthi123@kluniversity.in

Tel.: +91-8464933444

Copyright © 2022 Ukaaz Publications. All rights reserved. Email: ukaaz@yahoo.com; Website: www.ukaazpublications.com Chemical Co., Ltd developed the drug in Japan for the treatment of influenza A and B, and it is only approved for use in Japan (Ibrahim Bulduk, 2021).

Jyothi and Kavya (2021) established a single UV approach for favipiravir and concluded that the supplied spectrophotometric method should be used to estimate the novel antiviral repurposing medicine favipiravir because no simple UV spectrophotometric method for estimation has been disclosed. Favipiravir was developed and validated according to ICH principles since the medicine has a wide range of formulations that can be generated to treat different virus.

Dikma Technologies devised a simple HPLC-UV technique for simultaneous measurement of ivermectin, molnupiravir, remdesivir, favipiravir and ritonavir diamonsil® Plus C18 column (Kathiresan *et al.*, 2003; Megahed *et al.*, 2021; Shiraki and Daikoku, 2020).

The proposed approach was effectively implemented for the commercial formulations of favipiravir tablets, according to Nadendla and Patchala, who developed the HPLC method with a PDA detector (Nadendla and Abhinandana, 2021). Furthermore, the proposed method's key features are that it is cost-effective and environmen-tally friendly, with a retention time of nearly 4.622 min (Zhu *et al.*, 2019; Saber, 2020; Sohrabi, 2019).

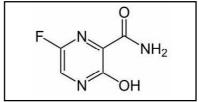


Figure 1: The structure of favipiravir.