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Application of Factorial Design for the Development of Site Specific Systems in the Management of Ulcerative Colitis.

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ABSTRACT

The objectives of the present investigation are to prepare and evaluate drug loaded sustained release matrix tablets for "ULCERATIVE COLITIS", using hydrophilic and hydrophobic polymers, by applying 2^3 factorial designs. The sustained release tablets of Mebeverine HCl were prepared employing different concentrations of HPMC K4M, HPMC K100M and Eudragit L100 in different combinations as a rate retarding polymer by wet granulation technique using 2^3 factorial designs. The quantity of polymers, HPMC K4M, HPMC K100M and Eudragit L100 required to achieve the desired drug release was selected as independent variables, X1, X2 and X3 respectively whereas, time required for 80% of drug dissolution (t_{80}%) was selected as dependent variables. Totally eight formulations were designed and are evaluated for hardness, friability, diameter, thickness, % drug content, *In-vitro* drug release and *In-vivo* studies. From the Results it was concluded that all the formulation were found to be within the Pharmacopoeia limits and the *In-vitro* dissolution profiles of all formulations were fitted in to different Kinetic models, the statistical parameters like intercept (a), slope (b) & regression coefficient (r) were calculated. Polynomial equations were developed for $t_{80\%}$. The formulation (F9) containing three polymers in optimized level using 2^3 factorial designs showed high $t_{80\%}$ value of 12 hours. The selected formulation (F9) follows Higuchi's kinetics, and the mechanism of drug release was found to be Anomalous type (Non-Fickian, n=0.896).

Keywords: Mebeverine HCL, 2^3 factorial designs, HPMC K4M, HPMC K100M and Eudragit L100.

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Review Article

A COMPREHENSIVE REVIEW ON HYDROGELS

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ABSTRACT

Polymers play a vital role in pharmaceutical development. Efforts have been continuously made to search a polymer that act in a controlled& desired way. Hydrogel development has solved many such issues. Hydrogels are hydrophilic, three-dimensional networks. Which are able to imbibe large amounts of water or biological fluids & thus resembles to a large extent, a biological tissue. They are insoluble due to the presence of physical or chemical crosslinks such as entanglements& crystallites. These materials can be synthesized to respond to a number of physiological stimuli present in the body, such as PH, ionic strength, temperature. The main aim of this article is to give a concise review on introduction, preparation methods, types, & various applications of hydrogels in the pharmaceutical field.

Keywords: Hydrogels, Types of hydrogels, Preparation methods, Applications.

INTRODUCTION

The existence of hydrogels dates back to 1960 when Wichterle and Lim first proposed the use of hydrophilic networks of poly (2-hydroxyethyl methacrylate) (PHEMA) in contact lenses. Since Then, the use of hydrogels has extended to various biomedical and pharmaceutical applications. In comparison to other synthetic biomaterials, hydrogels resemble living tissues closely in their Physical properties because of their relatively high water content and soft and rubbery Consistency. Several terms have been coined for hydrogels, such as intelligent gels (or) smart gels. Hydrogels are 'smart' or 'intelligent' in the sense that they can perceive the prevailing stimuli and respond by exhibiting changes in their physical or chemical behaviour, resulting in the release of entrapped drug in a controlled manner. By definition, hydrogels are polymeric networks with a three-dimensional configuration capable of imbibing high amounts of water or biological fluids.

Their affinity to absorb water is attributed to the presence of hydrophilic groups such as–OH,–CONH–,–CONH2–, and–SO3H in polymers forming hydrogel structures. Due to the contribution of these groups and domains in the network, the polymer is thus hydrated to different degrees (sometimes, more than 90%wt.), depending on the nature of the aqueous environment and polymer composition. Hydrogels show a swelling behaviour instead of being dissolved in the aqueous surrounding environment as a consequence of the critical crosslink's present in the hydrogel structure. These crosslink's are of two main categories including I) physical (entanglements or crystallites), and ii) chemical (tie-points and junctions). The crosslink's in the polymer network are due to covalent bonds, hydrogen binding, Vander Waals interactions, or physical entanglements [1, 2].

General benefits of hydrogels [3, 4]

- Biocompatible
- Can be injected *in vivo* (in a whole, living organism) as a liquid that then gels at body temperature
- Protect cells
- Good transport properties (such as nutrients to cells or cell products from cells)
- Timed release of medicines or nutrients
- Easy to modify
- Can be biodegradable or bioabsorbable.

General limitations of hydrogels [5-8]

- High cost
- Low mechanical strength
- Can be hard to handle
- Difficult to load with drugs/nutrients
- May be difficult to sterilize
- Non-adherent.

Hydrogel technical features [9]

The functional features of an ideal hydrogel material can be listed as follows:

- The highest absorption capacity (maximum equilibrium swelling) in saline.
- The desired rate of absorption (preferred particle size and porosity) depending on the application requirement.
- The highest absorbency under load (AUL).
- The lowest soluble content and residual monomer.
- The lowest price.
- The highest durability and stability in the swelling environment and during the storage.
- The highest biodegradability without formation of toxic species following the degradation.
- PH-neutrality after swelling in water.
- Colourlessness, odorlessness, and absolutely non-toxic.
- Photostability.
- Re-wetting capability (if required) the hydrogel has to be able to give back the imbibed solution or to maintain it;
- Depending on the application requirement (e. g., in agricultural or hygienic applications).

Preparation methods of hydrogels

1. Use of crosslinkers

- Copolymerization of monomers using multifunctional co-monomer, which acts as cross Linking agent, chemical initiator

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Original Article

A NOVEL FORMULATION OF CELECOXIB IN THE TREATMENT OF FAMILIAL ADENOMATOUS POLYPOSIS

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ABSTRACT

In the present study, an attempt was made to prepare celecoxib modified release tablets using a controlled release polymer HPMCK4M and an enteric polymer Eudragit L100-55 in the treatment of Familial Adenomatous Polyposis (FAP) a condition where numerous polyps mainly in the large intestine are present, which may be cancerous. According to European Medicines agencies celecoxib can be used to treat FAP, so tablets were prepared using varying concentrations of polymers by direct compression method. The selected polymers were found to be compatible as proven by FTIR study. Pre compression and post compression parameters data was found to be satisfactory and *in vitro* dissolution data proved that formulation F3 exhibited prolonged drug release for 6 hrs in intestinal pH where the drug was expected to release to treat intestinal polyps. Enteric polymer use prevented the drug release in stomach region pH as shown by the *in vitro* dissolution data.

INTRODUCTION

In the area of oral delivery, a growing attention has been given over the past few decades on the design and manufacturing of advanced formulations intended for release of bioactive compounds to selected regions of the gastrointestinal tract. By controlling the site of drug liberation throughout the gut, it would be possible to limit the tolerability issues associated with treatments that mainly affect specific GI districts, enhance the bioavailability of drugs that regional differences in their stability and/or permeability profiles or, alternatively, improve the therapeutic outcome in the management of widespread local pathologies (e.g. phlogosis, ulcers, microbial infections, motility disorders). Due to inherent anatomical characteristics and physiological role, the colon has long been considered unsuitable for absorption of substrates other than water or small inorganic ions and, consequently not viable as a release site for systemically acting drugs. However, it has been representing as elective GI region for targeted delivery of locally acting molecules. Currently the benefits sulting from selective release of steroidal and non steroidal anti inflammatory drugs into the large bowel are well recognized and widely exploited in clinics for the long term therapy of IBD, including crohn's disease, ulcerative colitis.[1]

Familial Adenomatous Polyposis (FAP), also known as familial polyposis coli, is a hereditary disease characterized by the progressive appearance of numerous polyps mainly in the large intestine. Polyps develop as early as in childhood. The average number of polyps in FAP patients is around 1,000, but this may vary between 100 and 2,500. Polyps are initially benign but can easily become cancerous. FAP may lead to cancer of the large intestine, and as such is a life-threatening condition. Available therapeutic methods consisted of endoscopic surveillance with removal of polyps when required. Prophylactic surgery to remove a part of the large intestine is performed if the polyps are numerous or the polyps are becoming cancerous. The patients also receive genetic counselling as the disease is inherited.[2] Celecoxib is an anti-inflammatory medicine. Its mode of action has been attributed to the inhibition of prostaglandin synthesis, via inhibition of an enzyme (protein molecules that act as catalysts in the cells biochemical reactions) called cyclooxygenase-2 (COX-2). Prostaglandins are a class of hormone-like (chemical messenger) lipids (fats) present in tissues and bodily fluids.

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Herbs Used As a Cure For Rheumatiod Arhritis : A Review

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ABSTRACT

Rheumatoid arthritis is chronic, progressive, disabling autoimmune disease characterized by systemic inflammation of joints, damaging cartilage and bone around the joints. It is a systemic disease which means that it can affect the whole body and internal organs such as lungs, heart and eyes. Although numbers of synthetic drugs are being used as standard treatment for rheumatoid arthritis but they have adverse effect that can compromise the therapeutic treatment. Unfortunately, there is still no effective known medicinal treatment that cures rheumatoid arthritis as the modern medicine can only treat the symptoms of this disease that means to relieve pain and inflammation of joints. It is possible to use the herbs and plants in various forms in order to relieve the pain and inflammation in the joints. There are so many medicinal plants that have shown anti rheumatoid arthritis properties. So the plants and plant product with significant advantages are used for the treatment of rheumatoid arthritis. The present review is focused on the medicinal plants having anti rheumatoid arthritis activity which are widely used in regular life in India.

Introduction

Rheumatoid arthritis is a systemic disease and it involve rheumatoid nodules, vacuities, eye inflammation, cardio pulmonary disease are manifestation of the disease. Rheumatoid arthritis is not an inherited disease. Researchers believe that some people have genes that make them susceptible to the disease. People with these genes will not automatically develop rheumatoid arthritis. There is usually a "trigger," such as an infection or environmental factor, which activates the genes. When the body is exposed to this trigger, the immune system responds inappropriately. Instead of protecting the joint, the immune system begins to produce substances that attack the joint. This is what may lead to the development of rheumatoid arthritis. It is autoimmune disease which means the body's immune system mistakenly attack on healthy tissues. The normal joint lining is very thin and it has very few blood vessels in it but in the rheumatoid arthritis joints the lining is very thick and crowded with the white blood cells. The white blood cells secrete chemical substances like interleukin-1 (IL-1) and tumor necrosis factor alpha (TNF-alpha) that produce pain, joint swelling and joint damage.[1]

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Investigation of Ghatti Gum as a Carrier to develop Polymeric Blend Beads of Galantamine Hydrobromide

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Abstract: Polymeric-blend beads of ghatti gum with sodium alginate containing the drug, galantamine hydrobromide were prepared by varying the gum concentrations and cross linkers viz., $CaCl_2$ and $AlCl_3$. It was found that in comparison between $AlCl_3$ and $CaCl_2$, the particle size, percent yield and drug entrapment efficiency was greater in beads prepared by $AlCl_3$ as cross linking agent. Formulation SGF6 formulations showed high percent yield which may be attributed for higher concentration of ghatti gum. SEM photographs for the prepared formulation indicated that the beads were having smooth and crack-free surface. FTIR and DSC spectra indicated that galantamine hydrobromide has not undergone any chemical interaction with the polymers and excipients used. *In vitro* drug release data indicated that formulations SGF3, SGF5 and SGF6 showed a release of about 99, 98 and 94% at the end of 12 h indicating their suitability for showing a 12 h release profile. Mathematical model fitting indicated that the best-fit model for the formulations was peppas and the release of drug from the polymer matrix followed super case-II transport. Formulation SGF6 was found to be ideal and when subjected for stability studies showed that the drug was stable.
Keywords: Ghatti gum, beads, sodium alginate, galantamine hydrobromide.

Introduction

Natural polymers and their derivatives are widely used to prepare various pharmaceutical dosage forms. Natural polymers can be modified to have tailor-made materials for preparing drug delivery systems and thus can compete with synthetic materials which are widely available in the market [1]. Oral sustained release dosage forms (DFs) are being developed for the past several decades due to their considerable therapeutic advantages [2, 3]. Natural polysaccharides hold advantages over synthetic polymers as they are non toxic, less expensive, biodegradable and easily available.

The use of biodegradable polysaccharides has gained importance in the development of controlled and sustained release drug delivery systems. Over the past few decades, natural biodegradable polysaccharides such as pectin, xanthan gum, guar gum, chitosan, carrageenans, sodium alginate (Na-alginate), hydroxypropyl methylcellulose (HPMC), agar and gellan gum have been widely used [4, 5]. These polymers can be exploited in various ways in the formulation of targeted and controlled drug delivery as they have different derivatizable groups, a wide range of molecular weight, and varying chemical composition. They can change their volume in contact with external media and form a viscous layer which serves as a protective barrier against water influx into

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KONJAC GLUCOMANNAN, A PROMISING POLYSACCHARIDE FOR COLON RELEASE: A REVIEW

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ABSTCRAT

Konjac glucomannan (KGM), a naturally occurring polysaccharide, has in recent years gained chain of β-D-glucose and β-D mannaose with attached acetyl groups in a molar ratio of 1.6:1 with β-1,4 linkages. It is commercially extracted from Kojac (*Amorphophallus konjac* or *Amorphophallus rivieri*) which is native to Asia. The KGM, by itself or by its gelling properties, was employed in pharmaceutical industry, health promotion and treatment. It has been used potentially as a increasingly in importance. The benefits of natural KGM are also more and more appreciated by scientists and consumer due to its biodegradability. KGM consists of a polysaccharide carrier for drug delivery to the colon, such as matrix tablets, gel beads, film-coated dose form. This review will discuss the important chemistry and general properties of glucomannan, and its gel formation mechanism and properties. The example of the pharmaceutical uses of KGM will be given.

KEYWORDS: Konjac glucomannan, polysaccharide, controlled release, colon.

INTRODUCTION

Konjac glucomannan is a high-molecular weight, water soluble, non-ionic, highly viscous, fermentable dietary fiber extracted from the tuber (or) root of the elephant yam, also known as Kojac (*Amorphophallus konjac* or *Amorphophallus rivieri*) which is native to Asia. KGM, is a naturally occurring biopolymer that is finding increasing applications in the pharmaceutical and biotechnology industry. It has been used successfully for many years in the food and beverage industry as a thickening agent, a gelling agent and a colloidal stabilizer. KGM also has several unique properties that have enabled it to be used as a matrix for the entrapment and/or delivery of a variety of drugs, proteins and cells. This review will first describe the source and production, chemical structure and general properties of KGM. The methods of gel formation and properties of the gels will then be discussed. Finally, some examples of the pharmaceutical uses of KGM will be given.

1. Glucomannan: origin and structure

Glucomannan (GM) is a polysaccharide of the mannan family, very abundant in nature, specifically in softwoods (hemicellulose), roots, tubers and many plant bulbs.[1-7] Despite the variety of sources, the most commonly used type of GM is named konjac GM, which is extracted from tubers of Amorphophallus konjac.[8,9]

Irrespective of its origin, Glucomannan consists of a polysaccharide chain of β-D-glucose and β-D-mannaose with attached acetyl groups in a molar ratio of 1.6:1 with β-1,4 linkages. Because human salivary and pancreatic amylase cannot split β-1,4 linkages, the degree of solubility is controlled by the presence of acetyl groups. Glucomannan passes relatively unchanged form into the colon, where it is highly fermented by resident bacteria. The molecular weight of KGM is ranging from 200,000 to 2,000,000 Da, which varies with origin, method of processing, and storage time. (Fig.1).[10] However, the man-nose/glucose monomer ratio may vary depending on the original source of GM. For example, it has been reported that konjac GM has a molar ratio of around 1.6:1, whereas GMs extracted from Scotch pine and orchid tubers have ratios of 2.1:1 and 3.6:1, respectively.[4,11] These values should be regarded cautiously given the variability observed depending on the studies and, in particular, on the analytical procedures.

In addition regarding the variable glucose/mannose ratio, the diverse types of GM may differ in their acetylation degree. The typical acetylation degree values are 5–10%. On the other hand, it is known that native GM can be easily acetylated with acetic anhydride in the presence of a catalyst.[12-14]

RESEARCH ARTICLE

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Synthesis of Silver Nano Particles from Aqueous Extract of *Alpine galanga* (Willd) Rhizome

S T V Raghavamma[1*], K Sasikala[1], N Sai Sreelekha[1], Mounika R[1], V Sasivadana[1], Rama Rao Nadendla[1]

Abstract: *Alpinia galanga* willd., (family - zingeberaceae), is a holistic gift of nature. It is a perineal herb found in Asia. The aqueous extract of its rhizome was used to produce pharmaceutically important silver nanoparticles. The formation of silver nanoparticles was confirmed by colour change from yellowish orange to dark red colour. Absorption spectra of UV analysis have shown maximum absorbance at 423 nm, for the particles obtained by process of sonication maximum absorbance was observed at a range of 220 nm. Absence of peaks in the range of 450 to 700 nm indicates absence of aggregation of silver nanoparticles. FTIR peaks were observed at 1639, 2987, 3248, 3538 cm^{-1}. SEM analysis resulted in particle size range of 50 to 70 nm. The X-ray diffraction pattern confirmed the amorphous nature of prepared silver nanoparticles. The nanoparticles synthesized were effective on organisms causing dental caries by producing a zone of 15.1 mm in case of microbes from dental swab and 14.3 mm in case of lactobacillus isolates.

INTRODUCTION

Nanoparticles are viewed as building blocks of fundamental nanotechnology. [1] Silver nanoparticles synthesized using various plant extracts are possessing antibacterial and antimicrobial activities. [2-5] The silver nanoparticles prepared can be characterized using UV, FT-IR, SEM and XRD studies. Based on these spectroscopic techniques the shape and size of nanoparticles can be studied. [6-11]

The species of the genus *Alpinia* used for synthesis of silver nanoparticles are *Alpinia purpurata* and *Alpinia calcarata*. Nanoparticles synthesized using *Alpinia purpurata* had shown anti bacterial activity and are highly resistant to multi drug pathogens. The size of nanoparticles produed using *A. purpurata* is in range of 28 to 32 nm. [12] AgNPs synthesized using *Alpinia calcarata* exhibited good nonlinear optical behavior and antimicrobial activities. [13]

In this research rhizome of plant *Alpinia galanga* belonging to the family Zingiberaceae was used for synthesis of silver nanoparticles. *Alpinia galanga* willd., is a perineal herb found in Asia. It is an official drug of ayurvedic medicine also known as galangal. Rhizome has characteristic fragrance as well as pungency. [14] The synthesized nanoparticles were tested for antimicrobial activity on dental swabs and on lactobacilli from milk for the first time to identify its application to prevent dental carries in children.

MATERIALS AND METHODS

Chemicals

Silver Nitrate, Peptone, Beef extract, Sodium chloride, Agar agar were purchased from Qualigens, Mumbai.

Plant Material

The Plant *Alpinia galanga* was identified based on the morphological characters and a voucher specimen was deposited in the herbarium. From this the rhizomes were collected by the process of digging and minced. These pieces were further used for the preparation of plant extract for synthesis of silver nanoparticles.

Preparation of *Alpinia galanga* Rhizome Extract and Silver Nanoparticles

The extract was prepared according to the standard procedure with slight modification. [10, 15] The rhizomes were freed from environmental impurities and cut into pieces. About 20 gm of fresh rhizomes were weighed using the digital balance. The minced material was added to 100 ml of boiling water. This solution was filtered by vacuum filtration process. The filtrate was further used for the synthesis of silver nanoparticles. The plant extract obtained was added to the 10^{-3} mM silver nitrate solution and placed in a water bath sonicator at 37°C for about 60 minutes. The formation of silver nanoparticles was monitored by analyzing the solution using UV-VIS Spectrophotometer. [1-11]

Characterization

The samples were collected at various time intervals like 0 min, 15 min, 30 min, 45 min and 60 min during the process of synthesis using water bath sonicator. These samples were subjected to spectrum scan in a UV-VIS spectrophotometer for knowing the maximum absorbance. [1-11, 16-22] The silver nanoparticles collected from the above process were characterized using spectroscopy, XRD and TEM analysis. The FTIR spectroscopic analysis was performed for the synthesized nanoparticles and scan was elucidated. TEM and XRD [17-24, 26] were used to analyze the parameters for nanoparticles.

Antimicrobial Activity

Antimicrobial activity of the synthesized nanoparticles was studies on dental swabs of infected dental samples and lactobacillus isolated from milk samples. The plague was collected and cultured on specific medium and antimicrobial activity was performed using disc plate method. [25]

RESULTS

The formation of silver nanoparticles was confirmed by colour change from yellowish orange to dark red colour.

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FORMULATION AND *IN-VITRO* EVALUATION OF A NOVEL BIODEGRADABLE POLYMER BASED MICROPARTICULATE SYSTEM FOR POTENTIAL COLON TARGETED DRUG DELIVERY

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Abstract:

The objective of present study is to design a novel multiparticulate system for colon targeting drug delivery system of cyclophosphamide (CPM) using biodegradable Konjac glucomannan (KGM) as a carrier for colorectal cancer treatment. Glucomannan is a high-molecular weight, water-soluble, non-ionic polysaccharide extracted from the tuber or root of the elephant yam, also known as konjac (Amorphophallus konjac or Amorphophallus rivieri). cyclophosphamide (CPM) has been the only agent with clinically active against colorectal cancer. Different batches of CPM granules were prepared and coated with KGM. Optimized CPM granules (KGM-STMP) were evaluated for flow properties, granular parameters, weight variation and content uniformity. The prepared formulations were subjected for in-vitro drug release studies in simulated gastric and intestinal fluids. It was found that during 2 hr at pH 1.2 HCl (SGF), 3 hr at pH 7.4 phosphate buffer (SIF) only less than 20% of drug was released. The drug release studies was also carried out in simulated colonic fluid (SCF) of pH 6.8 containing β-mannanase in order to mimic the conditions from mouth to colon. Drug release from 5-FU granules coated with KGM-STMP followed diffusion dependent zero order kinetics. Further, report suggested that konjac glucomannan (KGM) was biodegradable and susceptible to the colonic microfloras under anaerobic environments. Spectroscopic, (FTIR), X-ray Diffraction (X-RD) and DSC studies concluded that no polymer-drug interaction was concluded. Accelerated stability studies indicated that no significant changes, in drug release and micrometric patterns for observed when stored at 40± 2°C / 75±5% RH. Therefore, it was concluded that konjac glucomannan (KGM) is a promising potential carrier for targeting CPM in the vicinity of colon in order to treat colon cancer effectively.

Key words: *Cyclophosphamide (CPM), Konjac glucomannan (KGM), multiparticulate system, colon targeted.*

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FORMULATION AND EVALUATION OF GLIBENCLAMIDE ORAL FAST DISSOLVING FILMS

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ABSTRACT

The ultimate goal of any drug delivery system is the successful delivery of the drug, in which almost 90% of the drugs are administered to the body for the treatment of various disorders and diseases as it is regarded as the safest, most convenient and most economical method of drug delivery having the highest patient compliance. In this the drug is dissolved or swallowed and then enters into the systemic circulation to produce the desired effect. Despite of astounding advancement in drug delivery the oral route of drug administration is considered as the most important method of administration of drug for systemic effect because of self-medication, ease of administration and avoidance of pain compared to parenteral route. The aim of the present study is to formulate fast dissolving films of glibenclamide using HPMC K_4M, propylene glycol as a plasticizer, tween 80 as a surfactant, peppermint oil as flavouring agent and aspartame as sweetening agent. Glibenclamide solid dispersion of PEG 6000 is dispersed in the polymer solution. Films are prepared by solvent casting method and found to satisfy the mouth dissolving time and other film parameters. 2 x 2 cm of film is required to be placed on to patient tongue. Film instantly gets wet by saliva, rapidly hydrates, adheres to tongue and rapidly disintegrates and dissolves to release the drug for the oro – mucosal absorption or allow for gastrointestinal absorption to be achieved when swallowed. The formulated films exhibited acceptable film endurance. Time required for the film to dissolve and release 26 seconds and 2 minutes respectively. It can be concluded from the study that the oro – flash release film can be a potential novel drug dosage form for poorly water – soluble drugs.

KEY WORDS: Fast dissolving drug delivery, fast dissolving oral films (FDOFs), oral thin film (OTF), oro– flash release films, Glibenclamide, HPMC K_4M, solvent casting oro-mucosal absorption, poorly water soluble drugs.

INTRODUCTION

Oral delivery is the safest most convenient and economical method of the drug delivery having the patient compliance.[1] Fast dissolving drug delivery systems were first developed in the late 1970s as an alternative to tablets, capsules, and syrups for paediatric and geriatric patients who experience difficulties in swallowing traditional oral solid dosage forms.[2] Thin film drug delivery has emerged as an advanced alternative to the traditional tablet, capsules and liquid dosage forms. These drug delivery systems have advantages like increased bioavailability and to avoid first pass effect.[3] More recently, fast dissolving films are gaining interest as an alternative to fast dissolving tablets. Fast dissolving films disintegrate within 1-2 minutes when placed in mouth without drinking water or chewing.[4]

The mechanism of action of oral films is when they are placed on the patient tongue, films are Instantly wet by saliva due to the presence of hydrophilic polymer and other excipients the film rapidly hydrates and dissolves to release the medication for oral absorption.[5] Oral fast dissolving films are often prepared by solvent casting method and hot melt extrusion method.[4]

Glibenclamide is an oral hypoglycemic agent belonging to the second generation of sulfonylurea's used in the treatment of type II non-insulin-dependent diabetes. Its hypoglycemic effect is due to stimulation of insulin release from pancreatic beta cells and sensitization of the peripheral tissues to insulin. Glibenclamide is highly lipophilic (logP = 4.7) and poorly soluble in aqueous media. According to the Biopharmaceutical Classification Scheme (BCS), Glibenclamide comes under Class II drug, poorly soluble but able to permeate gastrointestinal
mucosa.[6]

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Inhibitory potential of important phytochemicals from *Pergularia daemia* (Forsk.) chiov., on snake venom (*Naja naja*)

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Abstract

Pergularia daemia (Forsk.) chiov., is a milk weed of Asclepiadaceae family. In the present study β-sitosterol, β-amyrin, α-amyrin and lupeol were identified in the leaf by GC–MS. Molecular docking studies were performed to evaluate their activities on phospholipase A2 (PLA2) and L-amino acid oxidase enzymes which constituted a rich source in snake venoms (*Naja naja*). Snake venom Phospholipase A2 with PDB code 1A3D devoid of co-crystallized ligand was extracted from Protein Data Bank. Using Molegro Virtual Docker two cavities are formed by cocrystallization. L-Amino acid oxidase (PDB code 4E0V) was a receptor model with a co-crystallized ligand FAD. Among the phytochemicals analysed, β-sitosterol displayed high affinity of binding to the active site regions of phospholipase A2 and L-amino acid oxidase, respectively. The affinity of binding was −125.939 and −157.521 kcal/mole identified by gold scores. α-Amyrin and β-amyrin had two hydrogen bond interactions with PLA2. Hence this study suggests that β-sitosterol identified in *P. daemia* can antagonize PLA2 and LAAO activities and forms a theoretical basis for the folk use of the plant against snake venom.

Keywords: *Pergularia daemia*, Snake venom, Phospholipase A2, L-Amino acid oxidase, Molecular docking

1. Introduction

Pergularia daemia is also called as Yugmaphala a perennial, small, twining herb with major pharmacological activities being reported on different parts of the plant. Arial shoots are known to possess anti-emetic and expectorant properties [1]. Singh et al. reported the probable use of plant parts

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Microwave-Assisted Synthesis and Biological Evaluation of 1, 5-Benzothiazepines as Potential Antihypertensive Agents

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ABSTRACT

A simple, rapid and highly efficient solvent-free synthesis of 2,3-Dihydro-1,5-benzothiazepines (BTZ 01-20) was carried out by the reaction of aryl chalcones with 2-aminothiophenol using silica gel as solid surface and zinc acetate as catalyst. The clean reaction conditions, shorter reaction time and high yields and purity of products are important advantages of this method. All the compounds were identified by melting point, TLC (R_f) and characterized by IR and ^1H-NMR spectral analysis. All the synthesized compounds were screened for antihypertensive activity. Hypertension was induced in male wistar albino rats by using fructose (66%), systolic and diastolic pressure (SBP, DBP) were measured on 16th day of administration of standard and test drugs by noninvasive BP system for rodents. Some of the compounds were found to possess significant antihypertensive activity in rat model.

Keywords: Aryl chalcones, 2-aminothiophenol, Microwave irradiation, 1,5-benzothiazepine, anti-hypertensive activity.

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Synthesis and biological evaluation of pyridopyrimidinone derivatives containing thiophene ring as potential anti-inflammatory and antimicrobial agents

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ABSTRACT

Thiophene is an important class of heterocyclic compound, has been shown to exhibit diverse biological and pharmacological activities such as anti-cancer, antioxidant, anti-inflammatory, antimicrobial, etc. In this study, a series of novel 2-Methyl-5-thiophen-7-(aryl-2-yl) pyrido[2,3-d]pyrimidin-4(3H)-one derivatives have been synthesized. All the synthesized compounds have been characterized by using elemental analysis, FT-IR, ^{1}H NMR, ^{13}C NMR spectroscopy and further supported by mass spectroscopy. Purity of all the compounds has been checked on thin layer chromatographic plate and HPLC technique. All the synthesized compounds were tested for their antibacterial and antifungal activity (MIC) in vitro by broth dilution method with two Gram-positive bacteria, two Gram-negative bacteria and two fungal strains. The biological activities of the synthesized compounds have been compared with standard drugs Ampicillin and Greseofulvin..The compounds exhibited significant antibacterial and moderate antifungal activities. These compounds can be further exploited to get the potent lead compounds. The detailed synthesis and the antimicrobial screening of the new compounds are reported.

Keywords: Pyridopyrimidinone, Thiophene, Antibacterial activity, Antifungal activity.

INTRODUCTION

It has been observed that spite of mounting problems of resistance to antimicrobial agents, the number of innovative antibiotics being brought to the pharmaceutical market have been reduced drastically in recent times.Here is shortage of novel antibiotics and appearance of multi-drug conflicting microbes being some of the major challenges for drug proposal and expansion of narrative antimicrobial agents.

Heterocyclic compounds containing sulphur have considerably a lot of attention due to wide application of pharmacological activity. Substituted thiophenes and their biheterocycles have received considerable attention during last two decades as they are endowed with wide range of therapeutic properties. A number of thiophene derivatives and Schiff bases have been reported to possess significant and diverse biological activities such as antibacterial [1, 2], antifungal [3, 4], antimicrobial [5, 6], anti-inflammatory [7,8],antioxidant [9, 10], antitumor [11, 12], Anti-leishmanial [13], antidepressant [14], antidiabetic [15], and local anesthetic [16] activities. Thiophene can be fused with various heterocyclic nuclei giving rise to newer compounds having enhanced biological activities.

In continuation to these efforts and with an objective to develop novel and potent therapeutic agents of synthetic origin, it was decided to synthesize certain 7-(Thiophen-2-yl)pyrido[2,3-d]pyrimidin-4(3H)-one derivatives and evaluate them for their antimicrobial potential.

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Synthesis of schiff bases bearing phenothiazine nucleus and their biological activities

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ABSTRACT

In the present study a series of novel Schiff bases which containing the Phenothiazine nucleus were synthesized (PD-1 to PD-10) by the condensation of the compounds N-methyl-10H-phenothiazine-3-carbaldehyde and different acylhydrazides in methanol and glacial acetic acid. All the synthesized compounds have been characterized by using elemental analysis, FT-IR, ^{1}H NMR, ^{13}C NMR spectroscopy and further supported by mass spectroscopy. Purity of all the compounds has been checked on thin layer chromatographic plate and HPLC technique. All the synthesized compounds were tested for their invitro antibacterial and antioxidant activities by agar diffusion plate method and DPPH free radical scavenging assay methods. All the synthesized compounds exhibited significant to moderate antibacterial and antioxidant activities. The results revealed that compound PD-7 exhibited significant antioxidant activity and the compounds PD-2, PD-5 and PD-8 exhibited good activity against S.aureus, E.coli, P. aeruginosa and B.subtilis and moderate activity against K. pneumonia. These compounds can be further exploited to get the potent lead compounds. The detailed synthesis and the antimicrobial screening of the new compounds are reported.

Keywords: Schiff bases, Phenothiazine, DPPH, Antioxidant, Antibacterial

INTRODUCTION

Increasing the resistance of microorganisms to currently available antimicrobial drugs is the major cause of morbidity and mortality throughout the world. Thus development of newer antimicrobial drugs is still in demand. The compounds carrying Azomethine functional group —C=N— which are known as Schiff bases have gained importance in medicinal and pharmaceutical fields due to the most versatile organic synthetic intermediates and also showing a broad range of biological activities, such as antitubercualr[1,2], anticancer[3-5], analgesic[6,7], anti-inflammatory[8,9], anticonvulsant[10,11], antibacterial[12], antifungal[13] antioxidant[14, 15], and anthelmintic[16] activities. The Schiff bases are good intermediates for the synthesis of many heterocyclic ring systems. The chemistry of Phenothiazine and its fused heterocyclic derivatives has received considerable attention owing to their synthetic and effective biological importance. In view of these and continuation of our biologically active molecules, we are hereby report the synthesis of some new Schiff bases bearing Phenothiazine ring and their *invitro* antioxidant and antibacterial studies.

MATERIALS AND METHODS

Melting points were determined in open capillary tubes and are uncorrected. Formation of the compounds was checked by TLC on silica gel-G plates of 0.5 mm thickness and spots were located by iodine and UV light. All compounds were purified by recrystallization with suitable organic solvents. IR spectra were recorded on Brooker-ALPHA FT-IR instrument using KBr pellet method. Mass spectra were recorded on Shimadzu GC-MS-QP-2010 model using direct inlet probe technique. ^{1}H NMR and ^{13}C NMR was determined in $CDCl_3$ solution on a Bruker Ac 400 MHz spectrometer. Purity of the synthesized compounds was checked by HPLC

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Bioanalytical Method Development and Validation of Ferrum in Rabbit Plasma Samples by Derivatised Reverse Phase Liquid Chromatography and Application to Pharmacokinetic Study

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Abstract

Iron is an important component of hemoglobin, in addition to other positive roles like proper growth and development of humans and for growing of fetus in pregnancy women. Iron deficiency anemia is more prevalent among vegetarian than non vegetarians. The purpose of this study was to develop and validate an bioanalytical technique for the estimation of iron levels in food samples (chicken liver, spinach, sprouts), in rabbit plasma by derivatised RP-HPLC by using 1-(2-pyridyl azo)-2-naphthol (PAN) as reagent. The separation was carried out using gradient elution with TAHS & acetonitrile with detection wave length at 280 nm. Grouping was done, each group contain 3 rabbits (same strain, weight, age). After overnight fasting, rabbits were fed with 100g of cooked spinach, sprouts and chicken liver with 240 mL of water. Blood samples were collected randomly at different time intervals upto 30 hrs. The plasma was separated and analyzed on basis of chromatographic conditions. The results showed the distribution of iron contents in various plasma samples. A high iron bioavailability was obtained from chicken liver sample when compared to spinach and sprouts. The method has been successfully applied to determine the trace levels of iron in biological samples with high precision & accuracy with sensitivity in less elution time of 3.2 ± 0.02 mins.

Keywords: PAN reagent; RP-HPLC; Iron

Introduction

Iron in general has poor availability from food derived from plant sources compared to food from animal sources. However, the Food and Nutrition Board of the National Research Council (National Research Council, 1989) has also stated that iron deficiency (anemia) appears to be highly prevalent among vegetarian women than among non-vegetarian women [1-3]. This was because in many studies of vegetarians in Western societies have found poorer iron status in vegetarian than in omnivores on the basis of measurements of hemoglobin, serum iron, iron binding capacity, or transferring saturation [4-8]. In this context further study of iron bioavailability in vegetarian diets is needed, because, several studies also suggested that vegetarians, compared to omnivores, have a greater risk of low iron status as indicated by lower concentration of serum ferritin [9-12]. This is because iron from plant derived foods is non-haem in nature which is markedly influenced by a greater number of dietary factors. It was also reported that lacto ovo vegetarian diet had 70% lower non-haem iron absorption than from non-vegetarian diet [13-17]. Majority of the Indian population with lower socio-economic status have to depend on foods from plant origin to satisfy their iron requirement, because of their poor purchasing capacity [18-22]. Their diet mostly constituted of cereals, millets, pulses and vegetables [23-25].

The most reliable method for determining bioavailability is measurement of absorption in human volunteer using radioisotopic technique, adoption of such technique involves ethical clearance. It is also expensive and needs elaborate experimental arrangements [26,27]. Considering the above aspects, the present study was designed to analyze various samples of spinach, sprouts and chicken liver for in-vivo availability of iron in rabbit blood by RP-HPLC.

Experimental

Instrumentation and Reagents

Instrumentation: Method development and validation was performed on Stainless steel Inertsil C_{18} (250 x 4.6 mm, 3.5 µ) column.

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Enantioselective method development and validation of proline by using high performance liquid chromatography

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Abstract

Chirality is a major concern in the modern pharmaceutical industry. The separation of chiral compounds has been of great interest because the majority of bioorganic and synthetic molecules are chiral. Aim of the present investigation was to develop a stereo specific, simple and precise normal phase high performance liquid chromatography (NP - HPLC) method for the separation and enantiopurity of Dextro (D) & Levo (L) enantiomers of proline (PRO) by using Lux 5µm Amylose – 1 LC column (250×4.6mm) by using n- Hexane: Iso propyl alcohol (IPA)as mobile phase in the ratios of 90:10 v/v at flow rate of 1.2 ml/ min. D & L forms of PRO was detected at 210nm with retention time of 8.1min and 9 min respectively with correlation coefficient (R^2) of 0.999.The method was validated with reference to International conference of harmonization (ICH) in terms of linearity, accuracy, precision (Inter - day and intra - day precision), limit of detection (LOD), limit of quantification (LOQ), stability of test solutions, specificity, system suitability, robustness and ruggedness.

Keywords: Enantiomers, enantioselective, enantiopurity, high performance liquid chromatography.

1. Introduction

Enantiomers are the two identical chemical molecules which differ each other by non-superimposable mirror images. Chirality of molecule depends upon the presence of one or more number of chiral centers or chiral plane or chiral axis etc. Different types of enantiomers were designated by various designations, it is done in accordance to Cahn – Ingold – Prelog for R and S systems. Octahedral structured molecules were designated by using Delta – Lambda. D and L Fisher – Ransoff should be used for the designation for amino acids and sugars. During 1980s: interest in the quantitative and qualitative estimation of enantiomers of the chemical moieties irrespective of their use was found to be important, due to variation in their activities. Enantiomers differ in their pharmacological activity, thereby estimation and separation of enantiomers got importance in the field of pharmaceutical analysis. Among all chromatographic techniques used HPLC is one of the best methods which can be used for the enantiopurity estimations and also for their separation with immobilized stationary phase. In the previous scenario enantiopurity was estimated by using achiral technique, by using chiral additives or chiral mobile phases and other method involves usage of auxillary chiral reagents which helps in the conversion of enantiomers into diastereomers there by enantiopurity can be determined by using reverse phase HPLC method. In the present scenario by using chiral stationary phase enatiopurity was estimated. Among all the chiral stationary phases, amylose and cellulose packed columns were most commonly used, due to wide range of applications. Resolution of peaks and separation of the enantiomers depends on the composition of mobile phase, pH and temperature of the column used. Proline is a natural nonessential amino acid which is synthesized by mammalian tissues it helps in the formation of collagen at joints and tendons. It is a nonpolar hydrophobic, hetero cyclic amino acid which is referred as imino acid which is part with 5 membered ring structures. Proline is available in 2 enantiomeric forms D and L forms. Among two forms L form is found to have key role in protein synthesis and also helps in normal physiological functioning of humans.

2. Experimental Conditions:

2.1 Materials Procurement:

Dextro (D) and Levo (L) forms of proline (PRO) was purchased from Sigma Aldrich and Isopropyl alcohol, n- Hexane and alcohol HPLC grade were purchased from Merck life science Pvt. Ltd, Mumbai.

2.2 Equipment:

Method development and validation was performed on HPLC, Mfg. by Agilent, model: 1200 infinity LC, with UV detector, amylose- 1 column (250mm × 4.6mm, 5µ) Phenomenex India Pvt Ltd was used for the separation and quantitative estimation. ATX - 224 analytical electronic balance was used for weighing Mfg. by Shimadzu, for pH measurement Titrasys - 352 model Mfg. By Systronics was used.

2.3 Chromatographic Conditions:

Enantiotropic separation was carried on Amylose-1 column, which is initially flushed with Iso Propyl Alcohol for 6 hrs at a flow rate of 0.5ml/min.

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NEWER SYNTHETIC APPROACHES OF BENZOTRIAZOLE DERIVATIVES

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ABSTRACT

Benzotriazole is one of the most important heterocyclic compound, having varied biological activities and still of great scientific interest now a days. They are widely found in bioorganic and medicinal chemistry with application in drug discovery. In the present study some newer benzotriazole derivatives were synthesized under conventional and ultra-sonication methods according to the scheme. All the synthesized benzotriazole derivatives have been characterized by using elemental analysis, FT-IR, ^{1}HNMR, ^{13}C NMR spectroscopy and further supported by mass spectroscopy. Purity of all the compounds has been checked on thin layer chromatographic plate and HPLC technique.

KEYWORDS: Benzotriazole, elemental analysis, FT-IR, ^{1}HNMR, ^{13}C NMR spectroscopy.

INTRODUCTION

Heterocyclic compound is one which possesses a cyclic structure with at least two different kinds of hetero atoms in the ring. Heterocyclic compounds are very widely distributed in nature and are essential to life in various ways. benzotriazole is a heterocyclic compound, having various biological activities and still of great scientific interest now a days. Benzotriazole possess interesting biological activities like anti-tumor[1], anti-microbial[2], anti-tubercular[3], anti-convulsant[4], anthelmintic[5], anti-oxidant[6], analgesic[7], anti-inflammatory[8], antifungal[9], antileishmanial[10], antipsychotic[11], anti-ulcer[12], local anesthetic[13] and schistosomicidal[14] activities. In the 1950s, a number of Benzotriazole derivatives were intensively studied, as the benzotriazole scaffold is one of privileged structure in medicinal chemistry.

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Synthesis and Biological Screening of Benzothiazole Derivatives with Pyrazole Moiety

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Keywords:
Pyrazole, Benzothiazole, Antimicrobial, Analgesic, Anti-pyretic

Abstract: Benzothiazole is one of the most important heterocyclic compound, weak base, having varied biological activities and still of great scientific interest now a days. They are widely found in bioorganic and medicinal chemistry with application in drug discovery. In the present study some novel benzothiazole derivatives were synthesized according to the scheme. All the synthesized benzothiazole derivatives have been characterized by using elemental analysis, FT-IR, ^{1}HNMR, ^{13}C NMR spectroscopy and further supported by mass spectroscopy. Purity of all the compounds has been checked on thin layer chromatographic plate and HPLC technique. All the synthesized compounds were tested for their antibacterial and antifungal activity (MIC) in vitro by broth dilution method with two Gram-positive bacteria, two Gram-negative bacteria and two fungal strains. The biological activities of the synthesized compounds have been compared with standard drugs Ciprofloxacin and Flucanazole. Analgesic activities were tested by Tail-flick method and Writhing method. The anti-pyretic activity was evaluated using Brewer's yeast induced pyrexia in rats. The compounds exhibited significant and moderate antibacterial, antifungal, analgesic and anti-pyretic activities. These compounds can be further exploited to get the potent lead compounds. The detailed synthesis and the antimicrobial screening of the new compounds are reported.

INTRODUCTION:

Heterocyclic compound is one which possesses a cyclic structure with at least two different kinds of heteroatoms in the ring. Heterocyclic compounds are very widely distributed in nature and are essential to life in various ways. Benzothiazole is a heterocyclic compound, weak base, is made from thiazole ring fused with benzene ring, having various biological activities and still of great scientific interest now a days. Benzothiazole possess interesting biological activities like anti-tumor (Yin GL et al, 2014), anti-microbial (Vikas S. Padalkar, 2011), anti-tubercular (Telvekar VN, 2011), anti-convulsant (Nadeem Siddiqui et al, 2012), anthelmintic (Balaji.P.N, 2014), anti-oxidant (Nagaraju G, 2015), analgesic (Govinda *et al, 2015*), anti-inflammatory (Achaiah, Garlapati et al, 2014), antifungal (Herrera Cano N, 2015), anti-leishmanial (Delmas F, 2004), antipsychotic (Gollapalli Naga Raju et al, 2015), anti-ulcer ((Gollapalli Naga Raju et al, 2015)), local anesthetic (Geronikaki A, 2009) and diuretic (Husain A, 2016) activities. In the 1950s, a number of benzothiazole derivatives were intensively studied, as the benzothiazole scaffold is one of privileged structure in medicinal chemistry. Based on these findings, synthesis of some compounds featuring benzothiazole derivatives fused with pyrazole moiety with the aim of obtaining more potent pharmacologically active compounds.

EXPERIMENTAL:

Material and Methods:

Melting points were determined in open capillary tubes and are uncorrected. Formation of the compounds was checked by TLC on silica gel-G plates of 0.5 mm thickness and spots were located by iodine and UV light. All compounds were purified by recrystallization with suitable organic solvents. IR spectra were recorded on Brooker-ALPHA FT-IR instrument using . KBr pellet method. Mass spectra were recorded on Shimadzu GC-MS-QP-2010 model using direct inlet probe technique. ^{1}H NMR and ^{13}C NMR was determined in $CDCl_3$ solution on a Bruker Ac 400 MHz spectrometer. Purity of the synthesized compounds was checked by HPLC Agilent. The results are in agreements with the structures assigned.

Synthesis of 7-chloro-6-fluorobenzo[d]thiazol-2-amine: 3-Chloro-4-fluoro aniline (3.7gm 0.025mol) mixed with potassium thiocyanate (20 gm 1.2mol) and glacial acetic acid (20 ml) in a three necked 250ml RBF with magnetic stirrer. The reactants are precooled to 0-5^{0}C by using freezing mixture. 30 ml of bromine water was added slowly by the help if funnel and maintain the temperature 0-5^{0}C. The mixture was further stirred 2hrs at 0-5^{0}C and 10 hrs at room temperature.

Synthesis of 1-(7-chloro-6-fluorobenzo[d]thiazol-2-yl)hydrazine: Hydrazine hydrate 5ml was placed in 100ml three necked RBF fitted with a mechanical stirrer and cool this to 5^{0}C using an ice bath. To the add 5ml concentrated HCl followed by 20ml ethylene glycol with continuous stirring and maintain the temperature 5^{0} – 10^{0} C. 7-chloro-6-

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Newer synthetic approaches of novel benzothiazole derivatives

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ABSTRACT

Benzothiazole is one of the most important heterocyclic compound, weak base, having varied biological activities and still of great scientific interest now a days. They are widely found in bioorganic and medicinal chemistry with application in drug discovery. In the present study some novel benzothiazole derivatives were synthesized under conventional and parallel synthesizer according to the scheme. All the synthesized benzothiazole derivatives have been characterized by using elemental analysis, FT-IR, ^{1}HNMR, ^{13}C NMR spectroscopy and further supported by mass spectroscopy. Purity of all the compounds has been checked on thin layer chromatographic plate and HPLC technique.

Key words: Parallel synthesizer, Benzothiazole, Antimicrobial, anti-oxidant, anti-tubercular

INTRODUCTION

Heterocyclic compound is one which possesses a cyclic structure with at least two different kinds of hetero atoms in the ring. Heterocyclic compounds are very widely distributed in nature and are essential to life in various ways. Benzothiazole is a heterocyclic compound, weak base, is made from thiazole ring fused with benzene ring, having various biological activities and still of great scientific interest now a days. Benzothiazole possess interesting biological activities like anti-tumor [1], anti-microbial [2], anti-tubercular [3], anti-convulsant [4], anthelmintic [5], anti-oxidant [6], analgesic [7], anti-inflammatory [8], antifungal [9], antileishmanial [10], antipsychotic [11], anti-ulcer [12], local anesthetic[13], schistosomicidal [14] and diuretic [15] activities. In the 1950s, a number of benzothiazole derivatives were intensively studied, as the benzothiazole scaffold is one of privileged structure in medicinal chemistry.

The conventional synthetic techniques have several drawbacks including usage of bulk amount of solvents, longer duration of time, low yields of products and usage of toxic substances etc. These are insufficient and harmful to environment. Environmental scientists supposed green techniques are micro-wave irradiation, ultra-sonication, phase transfer catalysis, parallel synthesizer and solvent free reactions. In the present work newer benzothiazole derivatives are compared with conventional and parallel synthesis methods and their spectral data also included.

MATERIALS AND METHODS

Melting points were determined in Digital melting point apparatus and are uncorrected. Formation of the compounds was checked by TLC on silica gel-G plates of 0.5 mm thickness and spots were located by iodine and UV light. All compounds were purified by recrystallization with suitable organic solvents.. All compounds were also synthesized in CAROUSEL six plus reaction station and as well as by conventional method. IR spectra were recorded on Brooker-ALPHA FT-IR instrument using KBr pellet method. Mass spectra were recorded on Shimadzu GC-MS-QP-2010 model using direct inlet probe technique. ^{1}H NMR and ^{13}C NMR was determined in $CDCl_3$ solution on a Bruker Ac 400 MHz spectrometer. Purity of the synthesized compounds was checked by HPLC Agilent. The results are in agreements with the structures assigned.

RESEARCH ARTICLE

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Synthesis, Characterization and Biological Screening of Novel Benzoxazolone Derivatives

Gollapalli Naga Raju[1*], Kondeti Tabu Naveen[2], Karumudi Bhavya Sai[2], Rama Rao Nadendla[1]

Abstract: Novel series of 5-Chloro-3-(3-substituted)-1,3-benzoxazol-2(3H)-one and 5-Chloro-3-[3-(cyclic amine)propyl]-1,3-benzoxazol-2(3H)-one derivatives were synthesized from 5-chloro-2(3H)-benzoxazolone with alkyl halides and 5-chloro-3-(3-substituted)-1,3-benzoxazol-2(3H)-one with 3-Cyclic amine substituted propyl chlorides. All the synthesized compounds have been characterized by using elemental analysis, FT-IR, ^{1}H NMR, ^{13}C NMR spectroscopy and further supported by mass spectroscopy. Purity of all the compounds has been checked on thin layer chromatographic plate and HPLC technique. All the synthesized compounds were tested for their antibacterial and antifungal activity (MIC) *in-vitro* by broth dilution method with two Gram-positive bacteria, two Gram-negative bacteria and two fungal strains. The biological activities of the synthesized compounds have been compared with standard drugs streptomycin and amphotericin-B. The compounds exhibited significant antibacterial and moderate antifungal activities. These compounds can be further exploited to get the potent lead compounds. The detailed synthesis and the antimicrobial screening of the new compounds are reported.

INTRODUCTION

2(*3H*)-Benzoxazolone heterocycles are considered 'privileged scaffolds' in the design of pharmacological probes. These heterocycles have, in fact, high versatility in chemical modifications, allowing changes to the characteristics of side-chains on a rigid platform. Studies designed to determine the mode of the biological action require the synthesis of many derivatives and in the last twenty years, this class of compounds has led to the discovery of a number of derivatives endowed with various biological activities like antimicrobial [1-3] anti-inflammatory, [4-6] analgesic, [7, 8] antitubercular, [9, 10] antioxidant, [11, 12] antimalarial, [13] anticancer [14-16] anticonvulsant, [17] anti-HIV, [18] antinociceptive [19, 20] etc.

Considering the above observations and in connection to previous publications involving the synthesis of new biologically active benzoxazolones. Therefore, this work deals with the synthesis of the 2(*3H*)-Benzoxazolone derivatives and screening their antimicrobial activities to investigate the effect of the alkyl group when placed in 3rd position of the benzoxazolone nucleus.

MATERIALS AND METHODS

2-Amino-4-chloro phenol was purchased from Merck, Mumbai. Concentrated HCl and CsF-Celite was purchased from Qualigens Fine Chemicals, Mumbai. THF from Loba Chem Ltd, Mumbai. Melting points were determined in open capillary tubes and are uncorrected. Formation of the compounds was checked by TLC on silica gel-G plates of 0.5 mm thickness and spots were located by iodine and UV light. All compounds were purified by recrystallization with suitable organic solvents. IR spectra were recorded on Brooker-ALPHA FT-IR instrument using KBr pellet method. Mass spectra were recorded on Shimadzu GC-MS-QP-2010 model using direct inlet probe technique. ^{1}H NMR and ^{13}C NMR was determined in $CDCl_3$ solution on a Bruker Ac 400 MHz spectrometer. Purity of the synthesized compounds was checked by HPLC Agilent. The results are in agreements with the structures assigned. Elemental analysis of the all the synthesized compounds was carried out on Euro EA 3000 elemental analyzer and the results are in agreements with the structures assigned.

Synthesis of 5-Chloro-2(3H)benzoxazolone

2-Amino-4-chloro phenol (14.35 g, 0.1 moles) was mixed with urea (30 g, 0.5 moles). Concentrated HCl (60 ml) was added carefully to the above mixture and was kept at 140°C for 2 hours then 170°C for 3 hours. After cooling, water (150 ml) was added and stirring was maintained for 1 h. The resulting precipitate was filtered, washed with water and crystallized from the ethanol. Yield 75%, white solid, M.P 193-194°C.

IR (KBr, cm^{-1}): 3157 (N-H), 3054 (=C-H), 1771 (-C=O), 1619, 1479 (-C=C), 1365 (-C-N), 1299, 1151 (-C=O), 804, 708 (=C-H ben). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 9.24-9.04 broad, 1H, NH), 7.37-7.04 (m, 3H, 3X Ar-H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 152.6, 140.4, 130.6, 129.5, 122.6, 110.2, 108.4. MS (*m/z*): 170 (M^+).

Preparation of the 5-Chloro-3-(3-substituted)-1,3-benzoxazol-2(3H)-ones (BX-1 to BX-5)

A mixture of 5-chloro-2(3H)-benzoxazolone (3 m. mol) and CsF-Celite (3 m.mol) in THF (7 ml) was stirred for 10 minutes under N_2 atmosphere. Alkyl halide (3 m. mol) in THF (3 ml) was added to the above mixture and stirred at ambient temperature for 10 hours. After completion of the reaction (TLC), CsF-Celite was filter off and washed with THF (2 × 5 ml). The combined organic layer was concentrated under vacuum and crystallized from ethanol to obtain pure product.

1. 5-Chloro-3-(3-chloropropyl)-1,3-benzoxazol-2(3H)-one (BX-1)

White solid, M.P 82-84°C. IR (KBr, cm^{-1}): 3063 (=C-H), 2933 (-C-H), 1774 (-C=O), 1611, 1485 -C=C), 1369 (-C N), 1247, 1061 (-C-O), 829, 721 (=C-H ben). MS (*m/z*): 246 (M^+). ^{1}H

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Synthesis, characterization and biological evaluation pyrazole derivatives containing indole ring as a potent analgesic and anti-inflammatory agents

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ABSTRACT

A novel series of pyrazole derivatives containing indole ring were synthesized from 1-Propyl-1H-indole-2-carbohydrazide and substituted chalcones were refluxed on an oil bath. All the synthesized compounds have been characterized by using elemental analysis, FT-IR, ^{1}H NMR, ^{13}C NMR spectroscopy and further supported by mass spectroscopy. Purity of all the compounds has been checked on thin layer chromatographic plate and HPLC technique. All the synthesized compounds were tested for their antibacterial and antifungal activity (MIC) in vitro by broth dilution method with two Gram-positive bacteria, two Gram-negative bacteria and two fungal strains. The biological activities of the synthesized compounds have been compared with standard drugs Ampicillin and Greseofulvin. The compounds exhibited significant antibacterial and moderate antifungal activities. These compounds can be further exploited to get the potent lead compounds. The detailed synthesis, anti-inflammatory, analgesic and antimicrobial screening of the new pyrazole derivatives containing indole ring are reported.

Keywords: Thiophene, Antibacterial activity, Antifungal activity.

INTRODUCTION

Indole is an aromatic heterocyclic organic compound. It has a bicyclic structure, consisting of a six membered benzene ring fused to a five-membered nitrogen-containing pyrrole ring. Indole alkaloids have been proved to be medicinally important natural compounds. Indole compounds include the plant hormone Auxin, the anti-inflammatory drug indomethacin, the β-blocker pindolol, and the naturally occurring hallucinogen dimethyltryptamine. The indole skeleton is one of the most attractive frameworks with a wide range of biological and pharmacological activities. Many researchers have described synthesis of indole and its derivatives along with its applications in literature. A large number of heterocyclic compounds containing the indole ring are associated with diverse pharmacological properties such as Analgesic [1], Antiallergic [2], Antibacterial [3], Anticonvulsant [4], Antifungal [5], Antihistaminic 6], Anti-inflammatory [7], Anticancer [8], Antiviral [9], Anthelminthic [10] and Anti-hypertensive [11].

Derivatives of pyrazole have played a crucial role in the history of heterocyclic chemistry and been used extensively important pharmacophores and synthons in the field of organic chemistry. Owing to their versatile chemotherapeutic importance, a significant amount of research effort has been focused on these nuclei. Pyrazole derivatives exhibit various biological activities such as, antibacterial [12], anticonvulsant [13], anticancer [14], anthelmintics [15], anti-inflammatory [16], herbicidal [17] and hypoglycemic [18] activities.

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Green Synthesis & Biological Evaluation of Novel Benzimidazole Derivatives as Antianxiety Agents

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Keywords:
Benzimidazole,
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Abstract: Benzimidazole is one of the most important heterocyclic compound, having varied biological activities and still of great scientific interest now a days. They are widely found in bioorganic and medicinal chemistry with application in drug discovery. In the present study some novel benzimidazole derivatives were synthesized under green synthesis by solvent free conditions by using catalytic amount of silica supported sodium hydrogen sulphate according to the scheme. All the synthesized benzimidazole derivatives have been characterized by using elemental analysis, FT-IR, ^{1}HNMR, ^{13}C NMR spectroscopy and further supported by Mass spectroscopy. Purity of all the compounds has been checked on thin layer chromatographic plate and HPLC technique. All the synthesized compounds were tested for their anti anxiety and neurotoxicity activities by elevated plus maze test in mice. Test compounds and diazepam was administered intraperitoneally in antianxiety study at dose of 2 mg/kg. Compounds BZ-6 & BZ-7 showed highest antianxiety activity compared to diazepam and did not show neurotoxicity in rotarod test. All the compounds exhibited moderate to significant antianxiety activity.

INTRODUCTION:

Heterocyclic compound is one which possesses a cyclic structure with at least two different kinds of hetero atoms in the ring. Heterocyclic compounds are very widely distributed in nature and are essential to life in various ways. benzimidazole is a heterocyclic compound, is made from imidazole ring fused with benzene ring, having various biological activities and still of great scientific interest now a days. Benzimidazole compounds and their derivatives were found to numerous pharmacological activities like antitumor (Nofal ZM *et al,* 2011), anticonvulsant (Bhanupriya Bhrigu *et al,* 2012), antimicrobial (Fatmah A. S. Alasmary *et al,* 2015), anthelmintic (Srikanth Lingala *et al,* 2011), anti-tubercular (Zhang HY, *et al*, 2014), schictosomicidal (Ríos N *et al.* 2013), antifungal (S. Khabnadideh *et al,* 2012), anti-inflammatory (Rajasekaran S *et al,* 2014), analgesic (Shobhit Srivastava *et al*, 2010), antioxidant (Subbegowda Rangappa *et al,* 2015) and anti-diabetic activities (Ramanatham Vinodkumar *et al,* 2008). The present research work focuses on the synthesis of newer benzimidazole derivatives under green synthesis by solvent free conditions by using catalytic amount of silica supported sodium hydrogen sulphate with potential activities that are now in development.

EXPERIMENTAL:

Material and Methods:

All the chemicals used were of laboratory grade and procured from E.Merck and S.D. Fine Chemicals (NSP, Guntur).The thin layer chromatography (TLC) was performed either using the Merck precoated TLC plates or on ACME's silica gel with 13% calcium sulphate ($CaSO_4$) as binder and the components were visualized under iodine chamber or by UV exposure or by the potassium permanganate ($KMnO_4$) spray technique. Flash column chromatography was performed using Merck silica gel (100-200 mesh). The chemicals and solvents were purchased from commercial suppliers either from Aldrich, Spectrochem, and Sisco research laboratories (SRL), Mumbai and they were used without purification prior to use. Melting points were determined in digital melting point apparatus and are uncorrected. All compounds were purified by recrystallization with suitable organic solvents. All the microwave experiments were performed using RAGA's microwave synthesizer. IR spectra were recorded on BROOKER-ALPHA FT-IR instrument using KBr pellet method. Mass spectra were recorded on Shimadzu GC-MS-QP-2010 model using direct inlet probe technique. ^{1}H NMR and ^{13}C NMR was determined in $CDCl_3$ solution on a BRUKER Ac 400 MHz spectrometer. Chemical shifts are expressed in δ ppm downfield from TMS as an internal standard. Purity of the synthesized

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Green synthesis, antiinflammatory and antimicrobial evaluation of novel isoxazole carboxamide derivatives

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ABSTRACT

Isoxazole derivatives possess antibacterial, antiviral, anti-fungal, anti-inflammatory insecticidal activities. The novel series of isoxazole carboxamide derivatives were prepared by the various ketene dithioacetals condensed with hydroxyl amine hydrochloride, potassium hydroxide under microwave irradiation. All the synthesized compounds have been characterized by using elemental analysis, FT-IR, ^{1}H NMR, ^{13}C NMR spectroscopy and further supported by mass spectroscopy. Purity of all the compounds has been checked on thin layer chromatographic plate and HPLC technique. All the synthesized compounds were tested for their antibacterial and antifungal activity in vitro by broth dilution method with two Gram-positive bacteria, two Gram-negative bacteria and two fungal strains. The biological activities of the synthesized compounds have been compared with standard drugs Streptomycin and Greseofulvin. The compounds exhibited significant antibacterial and moderate antifungal activities. These compounds can be further exploited to get the potent lead compounds. The detailed synthesis antimicrobial and anti-inflammatory screening of the new compounds are reported.

Keywords: Isoxazole, Anti-inflammatory, Antibacterial activity, Antifungal activity.

INTRODUCTION

The dramatically rising prevalence of multidrug-resistant microbial infection in the past few decades has become a serious health care problem. In order to prevent this serious medical problem, the elaboration of the new types of the previously known drugs is a very actual task. In recent years, the synthesis of novel isoxazole derivatives remains a main focus of medicinal research. Isoxazole is a five membered heterocyclic compound. Derivatives of isoxazole have played a crucial role in the history of heterocyclic chemistry and been used extensively important pharmacophores and synthons in the field of organic chemistry. Owing to their versatile chemotherapeutic importance, a significant amount of research effort has been focused on these nuclei. Isoxazole derivatives exhibit various biological activities such as antibacterial [1,2], anticonvulsant [3,4], anticancer [5-7], anthelmintics [8], anti-inflammatory [9-11], adenosine antagonist [12], fungicidal [13-15], herbicidal [16], hypoglycemic [17], muscle relaxant [18], nematocidal [19, 20], insecticidal [21], antiviral [22] and antimicrobial [23].

Considering the above observations and in connection to previous publications involving the synthesis of new biologically active isoxazoles. Therefore, this work deals with the synthesis of isoxazole carboxamide derivatives and screening their biological activities.

RESEARCH ARTICLE

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Synthesis and *In-vivo* Diuretic Evaluation of Novel Indole Carboxamide Derivatives

Gollapalli Naga Raju[1*], Karumudi Bhavya Sai[1], Kondeti T Naveen[2], Rama Rao Nadendla[1]

Abstract: Indole, the bicyclic ring system consists of pyrrole ring fused with benzene ring. Although indole moiety is very small but is fascinated by scientists because of the diverse biological activities by not only indole but its various substituted derivatives as well. In the present study some novel indole carboxamide derivatives like 6-Chloro-3-[(N,N-diethylamino)(oxo)acetyl]-1-methyl-N-aryl-1H-indole-5-carboxamide derivatives (IC-1 to IC-10) were synthesized according to the scheme. From all the synthesized novel indole carboxamide derivatives, IC-1 and IC-2 has been characterized by using elemental analysis, FT-IR, ^{1}HNMR, ^{13}C NMR spectroscopy and further supported by mass spectroscopy remaining are characterized by using elemental analysis, FT-IR, further supported by mass spectroscopy. Purity of all the compounds has been checked on thin layer chromatographic plate and HPLC technique. All the synthesized compounds were evaluated for *in-vivo* diuretic activity by collecting total excreted urine (0-5 hrs) of rat kept in metabolic cage. All the compounds exhibited moderate to significant diuretic activity.

INTRODUCTION

Heterocyclic compound is one which possesses a cyclic structure with at least one hetero atom in the ring. Heterocyclic compounds are very widely distributed in nature and are essential to life in various ways. The chemistry and biological study of heterocyclic compounds has been an interesting field for a long time in medicinal chemistry. A number of heterocyclic derivatives containing nitrogen atom serve as a unique and versatile scaffolds for experimental drug design. Indole is a heterocyclic compound, is made from pyrrole ring fused with benzene ring, having various biological activities and still of great scientific interest now a days. Indole compounds and their derivatives were found to numerous pharmacological activities like antitumor, [1] anticonvulsant, [2] antimicrobial, [3] anthelmintic, [4] antileishmanial, [5] antitubercular, [6] antioxidant, [7] antifungal, [8] anti-inflammatory, [9] antipsychotic, [10] antidepressant, [11] antimycobacterial, [12] cardiovascular activity, [13] analgesic, [14] anti-histaminic activity [15] and antibacterial [16] activities. The present research work focuses on the efficient synthesis of novel indole carboxamide derivatives and their biological evaluation as potent diuretic agents.

MATERIALS AND METHODS

All the chemicals used were of laboratory grade and procured from E Merck, Germany. Qualigens, Mumbai. Sigma Aldrich, USA and S.D. Fine Chemicals, Mumbai. Melting points were determined in digital melting point apparatus and are uncorrected. Formation of the compounds was checked by TLC on silica gel-G plates of 0.5 mm thickness and spots were located by iodine and UV light. All compounds were purified by recrystallization with suitable organic solvents. All the microwave experiments were performed using RAGA's microwave synthesizer. IR spectra were recorded on BROOKER-ALPHA FT-IR instrument using KBr pellet method. Mass spectra were recorded on Shimadzu GC-MS-QP-2010 model using direct inlet probe technique. ^{1}H-NMR and ^{13}C-NMR was determined in $CDCl_3$ solution on a BRUKER Ac 400 MHz spectrometer. Chemical shifts are expressed in δ-ppm downfield from TMS as an internal standard. Purity of the synthesized compounds was checked by HPLC AGILENT. The results are in agreements with the structures assigned. All chemicals were reagent grade and used without further purification and all solvents were freshly distilled before use.

Preparation of Methyl 6-chloro-3-[(*N*,*N*-diethylamino)(oxo)acetyl]-1-methyl-1*H*-indole-5-carboxylate

To a stirred cooled (ice bath) solution of methyl 6-chloro-1-methyl-1*H*-indole-5-carboxylate (0.5 gm, 2.34 m.mol) in dry DCM (12 ml), oxalyl chloride (0.95 ml, 11.21 m.mol) was added drop wise in solution. The obtained solution was stirred at 0°C for 30.0 minute and then at 25-30°C for 1 hour. Dark yellow colored was formed. The solvent was removed *in vacuo*, the residue was dissolved in dry DCM (12 ml) then add diethylamine (6.72 mmol) drop wise. The reaction mixture was stirred at 0°C for 30.0 minute and then 25-30°C for another 30.0 minute (monitored by TLC). The solvent was removed *in-vacuo*. The product was dissolved in water and extracted with ethylacetate (25 ml × 3). The combined organic layers were washed with water followed by brine and dried over anhydrous Na_2SO_4. The solvent was removed *in-vacuo* and the solid was triturated with hexane and resulting precipitate was filtered, washed with hexane and dried to give analytical pure product.

Preparation of Methyl 6-chloro-3-[(*N*,*N*-diethylamino)(oxo)acetyl]-1-methyl-1*H*-indole-5-Carboxylic Acid

To a stirred solution of methyl 6-chloro-3-[(diethylamino)(oxo)acetyl]-1-methyl-1*H*-indole-5-carboxylate (0.5 gm, 1.42 m.mol) in methanol (10 ml), 40% NaOH (1 ml) solution was added in solution. The reaction mixture was refluxed for 4 hour and the solvent was removed *in-vacuo*. The viscous oil obtained was neutralized with an aqueous solution of HCl. The product was extracted with ethylacetate (25 ml × 3) and the combined organic layers

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RESEARCH ARTICLE

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Synthesis and Anticonvulsant Activity of Some Novel Indole Carboxylate Derivatives

Gollapalli Naga Raju[1*], Karumudi Bhavya Sai[1], Kondeti T Naveen[2], Rama Rao Nadendla[1]

Abstract: Indole is one of the most important heterocyclic compound, weak base, having varied biological activities and still of great scientific interest now a days. They are widely found in bioorganic and medicinal chemistry with application in drug discovery. In the present study some novel indole carboxylate derivatives were synthesized under green synthesis by microwave irradiation method according to the scheme. Methyl 6-chloro-1H-indole-5-carboxylate was treated with CH_3I in presence of CS_2CO_3. Then Methyl 6-chloro-1H-indole-5-carboxylate was treated with oxalyl chloride in dry DCM and different secondary amines to get methyl 6-chloro-3-[(*N,N*-dialkylamino)(oxo)acetyl]-1-methyl-1H-indole-5-carboxylate derivatives (IND-1 to IND-10). IND-1 and IND-7 derivatives has been characterized by using elemental analysis, FT-IR, ^{1}HNMR, ^{13}C NMR spectroscopy and further supported by mass spectroscopy. Remaining derivatives were characterized by using elemental analysis, FT-IR and further supported by mass spectroscopy. Purity of all the compounds has been checked on thin layer chromatographic plate and HPLC technique. All the synthesized compounds were evaluated for anticonvulsant activity by maximal electroshock method (MES) by using phenytoin as standard at a concentration of 30 mg/kg. The anticonvulsant effect of the newly synthesized compounds was assessed by absence or reduction of hind limb tonic extensor phase. Among the synthesized derivatives compounds IND-5 and IND-10 were found to be the most potent compounds in the series.

INTRODUCTION

Indole is an aromatic heterocyclic organic compound. It has a bicyclic structure, consisting of a six-membered benzene ring fused to a five-membered nitrogen-containing pyrrole ring. Indole alkaloids have been proved to be medicinally important natural compounds. Indole compounds include the plant hormone Auxin, the anti-inflammatory drug indomethacin, the β-blocker pindolol and the naturally occurring hallucinogen dimethyltryptamine. The indole skeleton is one of the most attractive frameworks with a wide range of biological and pharmacological activities. This physiologically important nucleus is abundantly found in therapeutic agents as well as in natural products. Many researchers have described synthesis of indole and its derivatives along with its applications in literature. A large number of heterocyclic compounds containing the indole ring are associated with diverse pharmacological properties such as analgesic, [1] antiallergic, [2] antibacterial, [3] anticonvulsant, [4-5] antifungal, [6] antihistaminic, [7] anti-inflammatory, [8-10] anticancer, [11-12] antiviral, [13] anthelminthic, [14] antihypertensive [15] and antioxidant [16] activities. Thus the efficient synthesis of novel substituted indole carboxylate derivatives still represent highly pursued target.

MATERIALS AND METHODS

All the chemicals used were of laboratory grade and procured from E. Merck, Germany. Qualigens, Mumbai. Sigma Aldrich, USA and S.D. Fine Chemicals, Mumbai. Melting points were determined in digital melting point apparatus and are uncorrected. Formation of the compounds was checked by TLC on silica gel-G plates of 0.5 mm thickness and spots were located by iodine and UV light. All compounds were purified by recrystallization with suitable organic solvents. All the microwave experiments were performed using RAGA's microwave synthesizer. IR spectra were recorded on BROOKER-ALPHA FT-IR instrument using KBr pellet method. Mass spectra were recorded on Shimadzu GC-MS-QP-2010 model using direct inlet probe technique. ^{1}H NMR and ^{13}C NMR was determined in $CDCl_3$ solution on a BRUKER Ac 400 MHz spectrometer. Chemical shifts are expressed in δ ppm downfield from TMS as an internal standard. Purity of the synthesized compounds was checked by HPLC AGILENT. The results are in agreements with the structures assigned. All chemicals were reagent grade and used without further purification and all solvents were freshly distilled before use. All the synthesized compounds are evaluated for anticonvulsant activity by using maximal electroshock method (MES). The seizures were induced by SECOR INDIA electroconvulsiometer.

Preparation of Methyl 6-chloro-1-methyl-1*H*-indole-5-carboxylate

To a stirred suspension of CS_2CO_3 (2.72 gm, 0.02 mol) and methyl 6-chloro-1*H*-indole-5-carboxylate (2.09 gm, 0.01 mol) in dry DMF (10 ml), after 5 minute CH_3I (0.62 ml, 0.01 mol) was added drop wise. The resultant solution was stirred for 5 hour at room temperature and poured onto crushed ice, the product was isolated and washed withwater and hexane to give pure product. Yield: 95 %, M.P 60-61°C.

General Procedure for the Preparation of Methyl 6-chloro-3-[(*N,N*-dialkylamino)(oxo)acetyl]-1-methyl-1*H*-indole-5-carboxylates

To a stirred cooled (ice bath) solution of methyl 6-chloro-1-methyl-1*H*-indole-5-carboxylate (0.5 gm, 2.34 mmol) in dry DCM (12 ml), oxalyl chloride (0.95 ml, 11.21 mmol) was added drop wise in solution. The obtained solution was stirred at 0°C for 30.0 minute and then at 25-30°C for 1 hour. Dark yellow colored was formed. The solvent was removed *in-vacuo*, the residue was dissolved in dry DCM (12 ml) then add different secondary amines (6.72 mmol)

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Original Research Article

PHARMACOLOGICAL EVALUATION OF *PLUMBAGO ZEYLANCIA* LEAF EXTRACTS FOR ANXIOLYTIC ACTIVITY BY USING OPEN FIELD TEST

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Abstract: Treatment for various problems through herbal medicines is a traditional system being practiced for thousands of years. As all can obey the practice due to fewer side effects, considerable research on pharmacognosy, phytochemistry, pharmacology and clinical therapeutics has been carried out tremendously. Coming to the current research, on anti-anxiety or anxiolytic activity, most of the people in now a day have got feared in the present society due to many circumstances like stress, inferiority, backward in the hype areas in their own field. For this our basic research started with safe herbal extracts by using mice as experimental animals which are exposed on open field apparatus for evaluating anxiolytic activity. The current research got a good response as this procedure was very easy and fast for the evaluation.

Introduction: Herbal products are extensively used globally for the treatment of many diseases where allopathic fails or has severe side effects. Psycho neural drugs are also have very serious side effects like physical dependence, tolerance, deterioration of cognitive function and affect on respiratory, digestive and immune system. So in this contest the treatment through natural source is seen with the hope that they have the lesser side effects than that observed with synthetic drugs[1-4].

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Plumbago zeylanica L. is a multipurpose medicinal herb of family Plumbaginaceae. *P. zeylanica* is the most common plant used in Indian traditional system of medicine. A native of South Asia, the species is distributed throughout most of the tropics and subtropics; growing in deciduous woodland, savannas' and scrub lands from sea level up to 2000 m altitude. The root is used as laxative, expectorant, astringent, abortifacient and in dysentery[5]. Tincture of root bark is used as antiperiodic. The leaves are caustic and used in treatment of scabies. Plumbago is chemically characterized by the presence of naphthoquinones, flavonoids, terpenoids and steroids, many of them being responsible for several biodynamic activities. Popular name of *Plumbago zeylanica* is lead wort. This plant is

Evaluation of effects of *Commiphora Wightii* in Dehydroepiandrosterone (Dhea) induced Polystic Ovary Syndrome (Pcos) In Rats

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ABSTRACT

Background: Hyperandrogenism and insulin resistance are the main manifestations of polycystic ovary syndrome (PCOS), which appears to be caused by exposure to androgenized models have developed and investigated to study the etiology of polycystic ovary syndrome.

Objective: To evaluate the modulatory effects of *Commiphora wightii (C.wightii)* resins in response to hyperandrogenism in polycystic ovary syndrome.

Method: The animals were divided 18 adult (5-6 months old) wistar rats in to 4 groups the PCOS model was induced by daily administration of dehydroepiandrosterone (DHEA) 6mg/Kg in sesame oil p.o., up to 15 days and the rescue groups were take daily with metformin and *C.wightii* resin ethanolic extract 100mg/ kg in addition to DHEA. Serum glucose levels measured and steroid hormone levels were measured by fully automated bidirectionally interfaced chemi luminescent immunoassay. Samples were stained with hematoxylin and eosin for histological morphology.

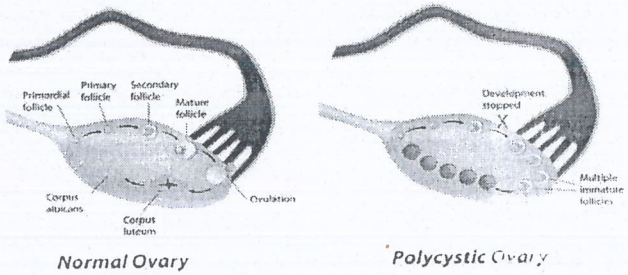
Results: The obtained results related to DHEA induced PCOS a significant ($P<0.05$) increase in hormone profile (estradiol, testosterone, progesterone, luteinizing hormone, follicle stimulated hormone) in PCOS rats in adult rats than the rescue groups. Furthermore glucose levels significantly (<0.05) elevated in PCOS rats compared with the other groups. The test treated ovaries had lower number of follicles compared to DHEA control group and similar to that of the control group than the standard.

Conclusion: *Commiphora wightii* resin has a potential role in reducing DHEA induced PCOS by reducing the morphological abnormalities of the ovarian follicles and normal hormone levels in adult rats.

Key words: dehydroepiandrosterone (DHEA), polycystic ovary syndrome (PCOS), *Commiphora wightii (C.wightii)*, histological morphology

INTRODUCTION

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders among women affecting 5– 10% of those of reproductive age. PCOS is characterized by hyperandrogenism, insulin insensitivity, and chronic anovulation.



Normal Ovary *Polycystic Ovary*

Figure no 1: difference in normal ovary and PCOS ovary

Research over the last few decades has established that Polycystic ovary syndrome is an important metabolic disorder, It has been proposed women who have mild hyperandrogenism and an isolated ultrasonic finding of polycystic ovaries but whose ovulatory function is maintained exhibit a mild form of Polycystic ovary syndrome. These women may be susceptible to developing the syndrome as well. Increased luteinizing hormone (LH) and increased insulin levels mainly amplify the intrinsic abnormality of their steroidogenesis. In PCOS, excess androgen activity may alter gonodotropins-induced estrogen

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Original Research Article

HEPATOPROTECTIVE EFFECT OF *JATROPHA CURCAS* FRUIT EXTRACTS AGAINST CARBON TETRACHLORIDE INDUCED LIVER FIBROSIS IN RATS

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ABSTRACT

The present study was undertaken to explore the hepatoprotective potential of *Jatropha curcas* fruit extracts against carbon tetrachloride (CCl_4) induced liver fibrosis in wistar rats. Liver fibrosis was induced by carbon tetrachloride (3ml/kg body weight) in animals. Blood biochemical, urine analysis and histological studies were carried to assess the hepatoprotective effect. Carbon tetrachloride administration induced severe liver fibrosis in rats, which was evident from enhanced levels of albumin, total bilirubin, direct bilirubin, indirect bilirubin, serum glutamate-O-methyl transferase, serum glutamate pyruvate transferase and alkaline phosphate. Pretreatment with silymarin (50mg/kg dose orally) significantly reversed carbon tetrachloride induced liver fibrosis. *Jatropha curcas* methanolic extract (250mg/kg body weight) showed significant effect than *Jatropha curcas* aqueous extract (250mg/kg body weight). From the obtained results it may be concluded that *Jatropha curcas* methanolic extract exerted a significant effect against CCl_4 induced hepatotoxicity in rats than *Jatropha curcas* aqueous extract ($p<0.001$) for most of the blood biochemical, urine analysis as well in attenuation of liver fibrosis.

Key Words: Hepatoprotective, Carbon tetrachloride, Silymarin, *Jatropha curcas,* Liver fibrosis.

INTRODUCTION

Liver is one of the major organs for biotransformation of drugs or chemicals. It not only helps in eliminating the therapeutically useful agents but also helps in the treatment of poisoning by enhancing the elimination of drugs or toxins. Certain drugs in excess dose or toxins through their reactive metabolites may cause liver injury because of the covalent or non covalent interactions with the liver cells. Therapeutically useful drugs like paracetamol, isoniazid, iproniazid, halothane, methotrexate, chlorpromazine, androgens, antimicrobials, certain toxins such as aflatoxins, carbon tetrachloride as well as alcohol can cause liver injury [1].

Silymarin is a bioflavonoid obtained from the ripe seeds of *Silybum marianum* (L) Gaerth which belongs to the family Asteraceae (Compositae). It is commonly found in western countries and India (Kashmir). In recent times this bioflavonoid is mainly used for its hepatoprotective effects. Its protective effects are mainly found to be due to its free radical scavenging activity, stimulation of RNA synthesis, stabilization of the membrane and hepatocyte repair mechanisms [2]. *Jatropha curcas* Linn (Family Euphorbiaceae) is a shrub found in Central America, Africa and India. Pharmacological studies on this plant has shown its usefulness in the treatment of influenza [3], bacterial infections [4], cancer [5], HIV [6], fungal infections [7], wounds [8], oedema [9], diarrhea [10], gynecological disorders [11], haemostatic disorders [12].

MATERIALS AND METHODS

Animals

Female wistar rats, weighing between 150 to 250 g were employed in the present study. They were obtained from animal house of Chalapathi Institute of Pharmaceutical Sciences, Guntur. The rats are provided with standard conditions (12 hr cycle;

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Research Article

CARDIOPROTECTIVE EFFECT OF *JATROPHA CURCAS* FRUIT EXTRACTS AGAINST CARBON TETRACHLORIDE INDUCED CARDIOTOXICITY IN RATS

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ABSTRACT

The present study was undertaken to explore the cardioprotective effect of *Jatropha curcas* fruit extracts against carbon tetrachloride induced cardiotoxicity in rats. Cardiotoxicity was induced by CCl_4 (3ml/kg body weight) in animals. Blood biochemical, hematological parameters and histopathological studies were carried to assess the cardioprotective effect. CCl_4 administration induced significant cardiotoxicity in rats, which was evident from enhanced levels of glucose, cholesterol, triglycerides and all hematological parameters. Pretreatment of silymarin (50mg/kg dose orally) significantly reversed carbon tetrachloride induced cardiotoxicity. From the obtained results it may be concluded that *Jatropha curcas* methanol extract (250mg/kg body weight) showed significant protective effect against CCl_4 induced cardiotoxicity in rats than *Jatropha curcas* aqueous extract ($p<0.001$) for most of the blood biochemical parameters, hematological parameters as well in attenuation of pathological changes in heart tissues.

Key words: Cardiotoxicity, cardio protective, carbon tetrachloride, silymarin, *Jatropha curcas*, *Curcas purgans*.

INTRODUCTION

Cardiovascular diseases (CVDs) are a group of disorders of the heart and blood vessels and they include: coronary heart disease – disease of the blood vessels supplying the heart muscle; cerebrovascular disease – disease of the blood vessels supplying the brain; peripheral arterial disease – disease of blood vessels supplying the arms and legs; rheumatic heart disease – damage to the heart muscle and heart valves from rheumatic fever, caused by streptococcal bacteria; congenital heart disease – malformations of heart structure existing at birth; deep vein thrombosis and pulmonary embolism – blood clots in the leg veins, which can dislodge and move to the heart and lungs.

CVDs are the number one cause of death globally: more people die annually from CVDs than from any other cause. An estimated 17.5 million people died from CVDs in 2012, representing 31% of all global deaths. Of these deaths, an estimated 7.4 million were due to coronary heart disease and 6.7 million were due to stroke. Over three quarters of CVD deaths take place in low- and middle income countries. Out of the 16 million deaths under the age of 70 due to non-communicable diseases, 82% are in low and middle income countries and 37% are caused by CVDs. Most cardiovascular diseases can be prevented by addressing behavioral risk factors such as tobacco use, unhealthy diet and obesity, physical inactivity and harmful use of alcohol using population-wide strategies. People with cardiovascular disease or who are at high cardiovascular risk (due to the presence of one or more risk factors such as hypertension, diabetes, hyperlipidaemia or already established disease) need early detection and management using counseling and medicines, as appropriate.

Clinical management of cardiovascular diseases is still a nightmare for the cardiologist. Thus far, vasodilators, β adrenergic blockers, antiarrhythmics, thrombolytics, etc. are the mainstay of cardiac therapy. Analgesic agents like morphine have also been used. Most of the currently used therapeutic interventions provide only symptomatic relief.

Despite advances in western system of medicine and medical technology world over, its increasingly being realized that if we have to support the healthcare requirements of our ever increasing population, we will have resort to economical, yet effective alternatives and there cannot be a better alternative than the herbal drugs which have had a long history of safe usage in different parts of the world, including India.

The attention of the world is now being drawn more and more to herbs and herbal medicines as the synthetic drugs seem to have come up against a wall in the treatment of illness which is described as life style diseases[1].

Silymarin is obtained from the *Silybum marianum* (milk thistle) an edible plant that has been used medicinally for the centuries as a herbal medicine. It is a mixture of mainly three flavonolignans, silybin, silidianin, and silychristine, with silybin being the most active. Silymarin has been used medicinally to treat liver disorders, because of its antioxidant activity and stimulation of ribosomal RNA polymerase and subsequent protein synthesis, leading to enhanced hepatocyte regeneration[2,3].

Jatropha curcas Linn. is a bush or small tree and belongs to Euphorbiaceae family. It is widely distributed in Mexico and Central America. The other name of the plant is *Curcas purgans*. Pharmacological reports revealed that it is having anti microbial[4,5,6], anti-inflammatory[7], antimetastatic[8], antitumor[8], coagulant and anti-coagulant (dose dependent), disinfectant, antiparasitic activity.

Research Article

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NEUROPROTECTIVE EFFECT OF BIOFLAVONOIDS AGAINST CARBON TETRACHLORIDE INDUCED NEUROTOXICITY IN RATS

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ABSTRACT

The present study was undertaken to explore the neuroprotective potential of bioflavonoids against carbon tetrachloride (CCl_4) induced neurotoxicity in rats. Neurotoxicity was induced by CCl_4 (3ml/kg body weight) in wistar rats. Blood biochemical, hematological parameters and histopathological studies were carried out to assess the neuroprotective effect. Administration of CCl_4 has induced significant neurotoxicity in rats, which was evident from enhanced levels of potassium and decreased levels of sodium. Pretreatment with quercetin (50 mg/kg dose orally) significantly reversed CCl_4 induced neurotoxicity than the silymarin (50 mg/kg dose orally). From the obtained results it can be concluded that quercetin exerted a significant neuroprotective effect against CCl_4 induced neurotoxicity in rats than silymarin ($p<0.001$) for sodium and potassium in blood biochemical parameters, packed cell volume, mean corpuscular hemoglobin count and red blood cells as well in attenuation of pathological changes in brain tissues.

Keywords: Neurotoxicity, bioflavonoid, carbon tetrachloride, quercetin, silymarin

INTRODUCTION

Flavonoids comprise a large group of chemical compounds with a basic diphenylpropane structure. They were divided into several subclasses like flavonols, flavons, flavanols and flavanons based on their functional groups. These compounds naturally occur in various plant parts (fruits, vegetables, nuts, seeds, flowers) and essential constituent of diet as well. Epidemiological studies indicated that diets rich in flavonoids were associated with reduced incidence of several chronic diseases including hepatic, renal diseases, asthma, type II diabetes and certain types of cancer. The neuroprotective properties of flavonoids were multi-faceted involving antioxidant and anti-inflammatory effects. The antioxidant property of flavonoids was thought, until relatively recently, to underlie the majority of their protective cellular effects. However, it is becoming increasingly apparent that flavonoids also influence cellular function by modulating the activity of many enzymes including the inhibition of protein kinases and lipid kinases[1].

Silymarin is a compound which is obtained from the plant *Silybum marianum* (milk thistle) was an edible plant it has been used medicinally for centuries as a herbal medicine. It is a mixture of mainly three flavonolignans: silybin, silidianin, and silychristine, with silybin being the most active. This compound has been used to treat liver disorders. The compound consistuent antioxidant activity, stimulation of ribosomal RNA polymerase and subsequent protein synthesis, lead to enhanced hepatocyte regeneration[2-5] .

Quercetin a major representative of the flavonol subclass, has received the considerable attention because of its overwhelming presence in foods. Quercetin and its sugar-bond or glucosylated, forms represent to 60-75% of flavonoids intake. It displayed the ability to prevent the oxidation of low-density lipoproteins (LDL) by scavenging free radicals and chelating transition metal ions. As a result, quercetin may aid in the prevention of certain diseases viz., cancer, atherosclerosis and chronic inflammation[6].

MATERIALS AND METHODS

Animals

Wister rats of either sex; weighing around 200- 250 g in the present study were the in-house breed of Chalapathi Institute of Pharmaceutical Sciences, Guntur. They were exposed to an alternate light and dark cycle of 12 hour period. During this period the animals were provided with a standard diet and water ad libitum. The animals were acclimatized to the laboratory conditions for at least 5 days before the neuro toxicity test. The experimental protocol was approved by the Institutional Animal Ethics Committee (IAEC) of Chalapathi Institute of Pharmaaceutical Sciences, Guntur, Andhra Pradesh (Approval No. 09/IAEC/CIPS/2016-17; dt 05/04/2016) and care of the animals was taken as per guidelines of the committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), Ministry of Forest, Environment, Climate Change, Government of India.

Drugs and reagents

Silymarin, quercetin was purchased from Sigma Aldrich, Bangalore, India. Carbon tetrachloride (CCl_4) and formalin were obtained from the Chalapathi Institute of Pharmaceutical Sciences. CCl_4 was administered intraperitonially (i.p.) to induce neurotoxicity in wistar rats[7,8].

Experimental groups

The efficacy of silymarin was compared with quercetin by evaluating in vivo neuroprotective activity in rats against CCl_4 induced neurotoxicity[9,10,11].

Four groups, each comprising of five wistar rats, were employed in the study. Group I (Control group): Rats were administered normal saline (0.9% w/v), orally for 14 days. Group II (CCl_4 - treated control group): Rats were administered CCl_4 (3 ml/kg,

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Effect of *Salix tetrasperma Roxburgh* Leaf Extracts on Central Nervous System Activities.

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ABSTRACT

The present study deals with investigation of leaf extracts of *Salix tetrasperma Roxburgh* was assessed for its CNS activities using neuropharmacological experimental models in mice. These activities are screened for ethanol and aqueous extracts at dose of 200 mg/kg and 400 mg/kg. Locomotor activity was measured by means of actophometer and skeletal muscle relaxant effect was evaluated by using rota rod apparatus. The results of the present study revealed both test extracts exhibited significant (P <0.001) activities in dose dependent manner in locomotor and muscle relaxant activity. From study it can be concluded leaf extracts of Salix tetrasperma Roxburgh possesses wide range of CNS activities.

Keywords: *Salix tetrasperma Roxburgh*, muscle relaxant, rota rod, actophotometer

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Original Research Article

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CARDIOPROTECTIVE EFFECT OF BIOFLAVONOIDS AGAINST ISOPROTERENOL INDUCED CARDIOTOXICITY IN RATS.

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ABSTRACT

The present study was undertaken to explore the cardioprotective potential of bioflavonoids against isoproterenol induced cardiotoxicity in rats. Cardiotoxicity was induced by isoproterenol (85mg/kg body weight) in animals. Blood biochemical, hematological parameters, urinalysis and histopathological studies were carried to assess the cardio protective effect. Isoproterenol administration induced significant cardiotoxicity in rats, which was evident from enhanced levels of glucose, cholesterol, triglycerides and calcium except sodium. Pretreatment with quercetin (50 mg/kg dose orally) significantly reversed isoproterenol induced cardiotoxicity than the silymarin (50 mg/kg dose orally). From the obtained results it may be concluded that quercetin exerted a significant cardioprotective effect against isoproterenol induced cardiotoxicity in rats than silymarin ($p<0.001$) for most of the blood biochemical parameters, mean corpuscular hemoglobin count as well as in attenuation of pathological changes in cardiac tissues.

KEYWORDS: Cardiotoxicity, bioflavonoid, isoproterenol, quercetin, silymarin, cardioprotective

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The International Journal of INDIAN PSYCHOLOGY

Reasons for Poor Medication Adherence in Patients with Depression

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ABSTRACT

Background: Depression is one among the disorders that have always been targeted by researchers in India. In South India the prevalence is 15.1%. Large number of studies has been published from India revealing various aspects of this commonly prevalent disorder, but there is limited evidence for the non-adherence to anti depressants in India. ***Aim:*** To assess the reasons contributing for non adherence in patients with depression. ***Method:*** This is a prospective, observational study, conducted in a tertiary care teaching hospital, Guntur. Medication adherence was assessed using the eight-item Morisky Medication Adherence Scale (MMAS-8) and a self administered questionnaire during the period of 1st February 2015 to 31st July 2015(i.e. 6months). ***Results:*** A total of 60 patients met the inclusion criteria; 68.3% are females and 31.6% are males. Among those, 3 (5%) are highly adherent, 17 (28.33%) are moderately adherent and 40 (66.67%) are poorly adherent. ***Conclusion:*** The overall Non adherence rate is found to be high in the study. The results presented suggest that pharmacist instructions may improve adherence in depression. Clinical pharmacist in this regard has a major role to play in uplifting and improving the quality of life of the patient.

Keywords: *Depression, Adherence, Non Adherence, Morisky Medication Adherence Scale, Self administered questionnaire.*

Anti depressants are commonly considered as a critical tool in the treatment of depression but they are useless if medication adherence is not improved. Although clinical guidelines recommend antidepressants be continued for at least 6 months after symptom remission, approximately one third of patients discontinue antidepressants within the first month of treatment, and 44% discontinue them by the third month of treatment. Poor adherence to antidepressant medications in depressive patients may lead to several complications like disease recurrence, relapse, increase in the cost of treatment, and impairment in daily functioning,

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Case Report

A Case Report on Pantoprazole Induced VIT.B_{12} Deficiency

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ABSTRACT

A 40 yr old male patient suffering with GERD was initially prescribed with Pantoprazole 40 mg OD for 15 days. After the treatment, suddenly the patient started feeling uncharacterized dizziness and fatigue. The patient consulted his physician who is a gastroenterologist. After a thorough examination the physician asked the patient for blood tests which revealed that the Hb is normal but the amount of Vit.B_{12} present in the blood is less than the normal. It was confirmed that, after the use of Pantoprazole, Vit.B_{12} blood levels have decreased which lead to the symptoms. This case report summarizes that on long term use of pantoprazole should be supported by supplemental therapy with Vit.B_{12}. **Background:** Proton pump inhibitors (PPI) are now one of the most widely used classes of drugs. PPIs have proven to have a very favourable safety profile and it is unusual for a patient to stop these drugs because of side effects. However, increasing numbers of patients are chronically taking PPIs for gastroesophageal reflux disease and a number of other common persistent conditions, therefore the long-term potential adverse effects are receiving increasing attention. One area that is receiving much attention and generally has been poorly studied is the long-term effects of chronic acid suppression on the absorption of vitamins and nutrients.

Key words: Pantoprazole, Gastroesophagal reflux disease, Gastric ulcer, Vitamin B_{12} Deficiency, Dizziness.

CASE PRESENTATION

An ADR report concerning a patient who developed vitamin B_{12} deficiency while being treated with pantoprazole. The patient, who had been treated with pantoprazole 40 mg for gastroesophageal reflux disease with gastric ulcer for 15 days. After this, the patient consulted his physician about uncharacteristic symptoms including periodic dizziness. Blood examinations revealed Vitamin B_{12} deficiency. The patient was examined, and no other causes were found that could explain the inability to absorb Vitamin B_{12}. After Pantoprazole was discontinued, serum B_{12} levels normalized.

TREATMENT

Withdrawal of the drug has relieved the patient from the unexplained periodic dizziness., and vitamin supplements was provided to that patient.

Outcome And Followup

The patient remained free of symptoms after he was given syrup Vit.B_{12}.

DISCUSSION

The proton pumps inhibitors (PPIs) as a class is remarkably safe and effective for persons with peptic ulcer disorders.[1] Anemia has frequently been reported as the only manifestation or the most frequent extra-intestinal symptom of celiac disease. Anemia due to isolated cobalamin deficiency is a frequent finding in the elderly, and its etiology goes beyond the classical pernicious anemia concept.[2] Deficiency of vitamin B_{12} is also common in CD and frequently results

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A MIRACULOUS HERBAL DRUG GINGER WITH ADDED THERAPEUTIC REMUNERATION

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ABSTRACT

Ginger an age old wonder household remedy useful for cooking and baking has also left its foot prints in the field of therapeutics. Research has demonstrated its long list of useful properties in various fields such as an antiemetic, antimotion sickness, antidiarrhoeal, antibacterial, antiinflammatory, analgesic, cholinergic and antipyretic. It also effectively reduces cholesterol levels and resists cholesterol build up as well as acts as a natural blood thinner that protects against strokes and blood clots. In addition, it is an inotropic and inhibits platelet aggregation there by promoting cardiovascular health. Ginger may also help alleviate chronic pain possibly by lowering levels of hormones that induce inflammation. Scientists have documented that ginger extract may slow the growth of colorectal and ovarian cancer cells and also inhibits cancer cell formation. Ginger also helps alleviate and minimizes mucous even helping asthmatics and also regarded as super food herb possessing antioxidant property. Keeping in mind the benefits of ginger can become a supportive measure in pharmacotherapy of various diseases.

KEYWORDS: Antimotion sickness, antidiarrhoeal, antibacterial, antiinflammatory, analgesic, cholinergic and antipyretic.

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APPRAISAL OF DIRECT COST OF TREATING EPILEPSY PER MONTH IN GUNTUR, ANDHRA PRADESH.

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ABSTRACT

OBJECTIVE: The aim of this study was to estimate in financial terms, the direct health care costs of treating epilepsy per month of clinic attendance and to relate these costs with the individual patients monthly income. METHODS: This is a cross sectional study conducted among inpatient attendees at the specialist pediatric service provided in secondary care hospital in Guntur, AP, from July 2015 to December 2015. RESULTS: A total of 120 patients were interviewed. 67% male child patients and 33% female child patients were included. The majority of patient's parents are employed. 48% patients were prescribed by the phenytoin, 31% patients were prescribed by the sodium valproate, in combination therapy 15% patients were prescribed by the both phenytoin+ sodium valproate. The biggest contributor was drug cost (9,991,800Rs). The direct cost of treating patients with epilepsy per month in 94 patients was 10,891,800Rs. The mean direct cost of epilepsy care determined from this study is 1,815,300Rs. CONCLUSION: Medication costs contributed the most to the direct costs of treating epilepsy. More than 45% of patient's parents on regular income spend 60% or more of their income in the treatment of epilepsy. Efforts towards reducing the direct cost of treating epilepsy should be directed towards mitigating the cost of the medications, transportation and service charges through appropriate policy interventions. In this study some ADR's were also observed.

KEY WORDS: Epilepsy, Pharmacoeconomics, Direct cost, Mean direct cost.

INTRODUCTION: Epilepsy is the most prevalent and serious neurological occurring in more than 50 million people worldwide[1]. Across Europe, 130,000 new cases of epilepsy are recorded each year among children and adolescents (an incidence rate of 70–80 per 100,000. The incidence is particularly high during the first year of life, and the likelihood of developing the condition then decreases during childhood. Anti-epileptic drug therapy is the primary treatment for children with epilepsy, with the aim of preventing seizures, and approximately 70% of patients become seizure-free with optimal drug therapy. Children who have severe, symptomatic epilepsy are those who are most commonly prescribed rescue medication. The longer a seizure continues increased risks of subsequent prolonged seizure activity, memory deficits and learning difficulties. In addition, the impact on health resources is greater because these patients require more intensive medical assistance. Then costs of direct medical care for children with epilepsy can be very high[17]. The choice of drugs varies considerably among physicians both within hospital and across the country. Prompt treatment with rescue medication is an important aspect of care for children experiencing PAC however, such treatment provides a particular challenge because these seizures occur predominantly in the community setting where rescue medication and trained careers may not always be available. Concerns about rising costs, unexplained variations in utilization, and limited information about long-term patient outcomes have ushered in an era of cost containment and accountability. At a time when a wealth of new epilepsy treatments has become available, payers increasingly demand evidence that the costs of treatments are justified by the scope of the problems and the outcomes they produce. Results of cost-effectiveness studies have influenced policy decisions in several European countries.

AIM AND OBJECTIVES: The aim of this study was to estimate in financial terms, the direct health care costs of treating epilepsy per month of clinic attendance and to relate these costs with the individual patient's monthly income. To identify the principal cost drivers and to estimate based on monthly costs the total cost per patient per six months.

METHODOLOGY

This study had a cross sectional design and was conducted among inpatients attendees at the specialist of pediatric department of secondary care hospital at Guntur

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Original Article

Measurement of Outcomes in Hypertensive Patients with Relation to Counselling

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ABSTRACT

Aim and objectives: the main aim of the study is to measure the outcomes in hypertensive patients with relation to, counselling in terms of lifestyle modifications, diet, risk factors, complications, signs and symptoms by providing patient information leaflet. The objective is to evaluate the impact of patient counseling in terms of QOL, KAP and medication adherence.

Materials and methods: an observational prospective study was conducted over a period of 6months i.e., from february to july 2015 in the department of general medicine, government general hospital, guntur. The patients were counseled and patient information leaflets were given for knowledge enhancement. Then the patients were assessed in terms of medication adherence, KAP and QOL by using validated questionnaires. Further follow ups and counseling were done on patient visits for their review or telephonically. Assessment of all collected data was statistically analyzed.

Results: a total of 134 hypertensive patients were included in the study but only 107 patients of them were enrolled in the study as per the inclusion and exclusion criteria and counseling was done. The p value in terms of medication adherence and KAP was calculated and found to be *p = <0.0001, which is considered to be statistically significant. The QOL was found to be significantly improved in terms of anxiety/depression and pain/comfort.

Conclusion: our study concluded that pharmacist mediated patient counseling was effective in improving disease knowledge, drug compliance and quality of life.

Key words: Hypertension (HTN), patient counseling, patient information leaflets (pils) ,drug compliance, life style modification, quality of life.

1. INTRODUCTION

Hypertension is a very common chronic disease in rural, urban and semi urban areas of today's world, which needs continuous monitoring and treatment throughout the life. Hypertension is an important public health challenge because of the associated

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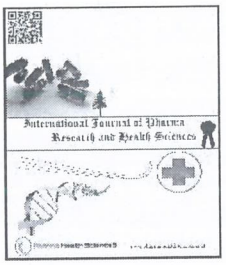

Original Article

The Role of Clinical Pharmacist in Reducing Medication Errors in Out Patient Counseling Department in a Secondary Care Hospital

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ABSTRACT

Introduction: Dispensing errors are believed to be the most prevalent type of medical error and are a significant cause of preventable adverse events. **Aim and Objective**: The aim of this study are to discuss the underlying factors in dispensing errors, health care uncertainty and therapeutic outcomes, and to identify the extent of human- and system-based sources of errors by exploring hospital pharmacists' attitudes and dispositions to die and uncertainties; and the implications for patient safety in a tertiary hospital. **Methodology:** A cross-sectional survey of clinical pharmacists in secondary care hospital in Guntur was conducted over a period of 4 months from october through january 2015. a stratified random sample of 64 patient's data was collected.these study was conducted in out patients department. **Results:** Out of 64 patients 34(54%) patients were male and 30(46%)patients were female. 41% patients were comes in the age range of 41-60 years .most of the errors (32) were observed in general medicine only. these errors are gradually decreased from october to january. **Conclusion:** In conclusion, majority of hospital pharmacists indicated that the risk of dispensing errors was increasing and most of them were aware of dispensing errors.the profession needs to be proactive and standards must be set appropriately high (i.e. zero error tolerance) clinical pharmacist must communicate with physicians , nursing staff and other hospital pharmacist thereby we can minimize the errors.

1. INTRODUCTION

Dispensing errors are defined as any inconsistencies or deviations from the prescription order such as dispensing the incorrect drug, dose, dosage form; wrong quantity; inappropriate, incorrect, or inadequate labeling, confusing, or inadequate directions for medication use; incorrect or inappropriate preparation, packaging, or storage or medication prior to dispensing (Szeinbach et al., 2007). Many prescription errors are made during the various phases of medication usage in the hospital environment; dispensation is one of the most sensitive phases of the

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NANO TECHNOLOGY: A NEW THERAPEUTIC APPROACH FOR DIABETES

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Abstract:

Nano technology an exciting area of scientific development offers ways to create smaller, cheaper, lighter devices that can help to do better. The current literature has recognized and reported many possibility and applications of nano technology. The medical applications of nano technology are tremendous and could give medicine including the treatment of diabetes a new therapeutic approach. The frequency of diabetes is growing rapidly all over the globe at an alarming rate. Hence, the application of nano technology plays a very vital role in diabetes. Nano technology is useful in detection of even very minute amounts of insulin and blood sugar levels in the body. The treatment of diabetes includes proper delivery of insulin into blood stream which can be attained by nano technology by developing oral insulin which can make patient comfortable and patient compliance. Development of artificial pancreas can also be accomplished by using nano technology. Silicon boxes can also be implanted under the skin of diabetic patient that could temporarily restore the bodies' glucose feedback loop. Without the need of powerful immunosuppressant's that is acquired by nano technology. Another important approach of nano technology is a nano pump which injects insulin to the patient's body at a constant rate balancing the amount of sugar in blood. And also can administer the small drug doses over a prolong period of time. Therefore, nano technology a new mode of treatment may help in making the everyday lives of millions of diabetics patients more tolerable.

Key words: *Diabetes mellitus, nanotechnology and nanoparticals.*

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Study on Effectiveness of Adding Phenobarbitone to Conventional Therapy in Preterm Neonates with Unconjugated Hyperbiliurubinemia in Comparison with Conventional Therapy

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Authors' contributions

Authors are contributed in this study as well as the direction of corresponding author and with the support of the department of pediatrics.

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Original Research Article

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ABSTRACT

Aim: To assess the effectiveness of adding prophylactic phenobarbitone to conventional therapy in preterm neonatal jaundice in reducing the incidence, peak serum bilirubin levels, duration and need of Phototherapy in the treatment and time taken for complete clearance of jaundice.
Background: Neonatal unconjugated hyperbilirubinemia is a life threatening. The conventional therapy is a long time process & some of neonate cannot tolerate for long-term phototherapy. Adding of phenobarbitone to the conventional therapy gives better results.
Study Design: A prospective observational study in comparison with retrospective data & it was conducted in the 6 months period i.e., from February 2015 to July 2015 at GGH guntur.

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