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Evaluation of in Vitro and in Silico Anti-Inflammatory Potential of Some Bioactive Compound from Annona Squamosa through Docking Approach

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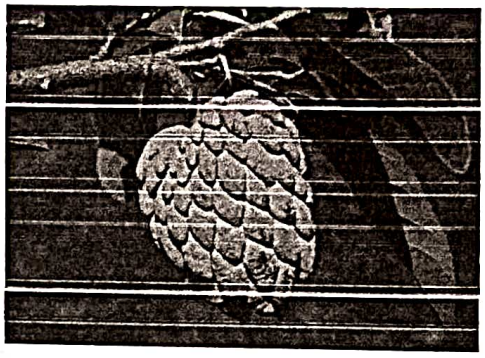
Abstract— Annona squamosa Linn is a versatile tree with edible fruits & a source of the medicinal & industrial products. A.squamosa Linn is used as an antioxidant, hepatoprotective, antidiabetics, cytotoxicactivity, genetoxicity, antitumor activity. Flavonoids are major active constituents found in the leaves of A. squamosa and have been used to treatment of various human diseases. Rutin (quercetin-3-rhamnosyl glucoside) and Quercetin as the flavonoids exhibited anticancer, antiviral, anti-inflammatory and heart disease protective activities. Rutin by acting as antioxidants exhibited several beneficial effects, such as anti-inflammatory, anti-allergic, anti- viral as well as an anticancer activity. This study aimed to predict the ability of flavonoids from the A. squamosa in inhibition COX-2 enzyme as a prostaglandin source. In the present study an attempt had been made for docking simulation for 2 compounds was executed through Autodock Vina. All the calculations were carried out by using Autodock4.2 as docking tool. The visualization and other programs necessary for docking studies were performed out by means of Pymol, Chimera, DS visualizer, MMP Plus.

Keywords— *A.squamosa, Rutin, Quercetin, Molecular docking & binding energy.*

I. INTRODUCTION

The therapeutic efficacy of many indigenous plants, for diverse diseases has been defined with the aid of conventional herbal medicinal practitioners[1]. Annona squamosa (A. squamosa) L. (Family: Annonaceae), generally known as custard apple[2].



Annona squamosa

The main flavonoids found the leaves of A.squamosa are quercetin-3-O robinobioside, rutin, quercetin-3-O-β-D-glucoside, kaempferol-3-O-robinobioside, and kaempferol-3-O-rutinoside[3].

Description of Active Flavonoids		Therapeutic uses
Rutin	Rutin is a flavonoid gift inside the plant nation as allelopathic substances. Rutin is the rhamnoglucoside of the flavonoid quercetin an located in many flora and used for treatment of diverse diseases related to the related to the Vascularity[4]. It is quercetin-3-rutinoside or 3,3',4', 5,7-pentahydroxy flavones-3-rutinoside and has a chemical formula C27H30O16.	Conventionally, it's miles used as antimicrobial, antifungal, and antiallergic agent. However, cutting-edge research has proven its multi-spectrum pharmacological advantages for the remedy of various continual diseases inclusive of cancer, diabetes, high blood pressure and

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Research Article

Nootropic Activity of Ethanolic Extract of Alangium Salvifolium in Acute and Chronic Stress Induced Wistar Albino Rats

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ABSTRACT
Objectives- The present study was designed to evaluate the nootropic activity of ethanolic extract of Alangium salvifolium (ASE) on stressed wistar albino rats. Materials and methods- Effect of ASE was studied on acute restraint stress and chronic unpredictable stress induced rats. Chronic unpredictable stress was given for 10days. The reference standard drug (Piracetam-200mg/kg) and the test drug, ASE at doses of 150mg/kg and 200mg/kg b.w. were given to rats for 14 days. Learning and memory was assessed by using Elevated plus maze test. Animals sacrificed at the end of this experiment, the body weight adrenal and spleen weight, ulcer index as well as various biochemical parameters like malondialdehyde (MDA) and superoxide dismutase (SOD) were assessed. Results- Both acute as well as chronic stress induced a significant prolongation of learning time, whereas only with chronic unpredictable stress the memory or retention time was longer than that of the non-stressed control rats. Piracetam and ASE treated rats showed a significant reduction in acquisition and retention time in stress induced rats. Also, the stress induced ulcer scores were significantly reduced. The effects were comparable to normal control rats. Conclusion- In our study we found that ASE restored the stress induced impaired cognition which suggests its nootropic activity.

Keywords: stress, Alangium salvifolium, transfer latency, ulcer index.

INTRODUCTION

Stress has become a regular feature of life today, yet there is a considerable ambiguity in the meaning of this word. In common usage, stress usually refers to an event or succession of events that cause a response, often in the form of distress. Stress targets nervous system along with the immune system, metabolic and cardiovascular system etc which are affected by both adaptive and mal- adaptive responses to stress [1].

Stress induced generation of reactive oxygen species (ROS) in brain is a contributing factor for alteration in motor, visceral, endocrine and behavioural performances. So, many researchers have explained that anti-oxidants ameliorate neurobehavioural and endocrine function by counteracting oxidative damage [2]. Alangium salvifolium, commonly known as wheat grass has been used since ancient times in folk medicine for its medicinal properties. A number of scientific reports show that juice of wheat grass has potent anti-ulcer [3], antioxidant [4], anti- arthritic [5], antidiabetic [6] effects. Recently its neuroprotective effect on β- amyloid induced cell death and memory impairment has been studied in rats [7]. Hence the present study was undertaken to evaluate the nootropic effect of ethanolic extract of the test drug, Alangium salvifolium against stress in wistar albino rats.

METHODOLOGY

In the present study, fifty four (54) wistar albino rats of either sex weighing between 100-150 gm were selected. The animals were randomly divided into nine
(9) different groups of six in each (n=6). All animals were hygienically housed at room temperature and under standard laboratory condition of 12hr light and dark cycle in the animal house of department of pharmacology,Vaagdevi pharmacy college ,warangal. The study was conducted after taking permission from Institutional Animal Ethical Committee (IAEC). The study period was 6 months.

Before the experiment all animals were acclimatized to standard laboratory conditions for 7 days and had free access to food and water throughout the period of experiment. They were used only once in the experiment. All experiments

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Evaluation of Anti-Diarrhoeal Activity of Capparis Zeylanica Leaf Methanolic Extract in Albino Wistar Rats

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ABSTRACT

India has a dense forest with plenty of medicinal plants which have been used as folklore medicines by the local people for many years. They used different plant parts of Capparisspecies to treat diarrhoea. Depending on the traditional use of some plants of Capparisgenus as antidiarrhoeal, this plant was selected to evaluate antidiarrhoeal activity in animal models. Wistar albino rats weighing 180 to 200 grams were used in this study. There were five groups in each experimental model with six animals in each group. The antidiarrhoeal activity was evaluated by different experimental models namely castor oil-induced diarrhoeaand magnesium sulphate induced diarrhoea. The methanolic extract of Capparis zeylanica leaves showed significant antidiarrhoeal activity against castor oil-induced diarrhoea and magnesium sulphate induced diarrhoea in rats. The methanolic extracts at 100, 200 and 400 mg/kg significantly inhibited diarrhoea. There was a significant dose-dependent anti diarrhoeal effect in both the animal models as compared to the standard drug ($P<0.01$). Based on the results in experimental models, the methanolic extract of Capparis zeylanica demonstrated significant reductions in faecal output when compared to the standard groups. In conclusion it can be said that tannins and flavonoids present in the plant extracts may be responsible for the antidiarrhoeal activity.

Keywords: anti-diarrhoeal, experimental models, Capparis zeylanica, methanolic, wistar albino rats.

1. INTRODUCTION

Diarrhoea is a very common ailment and national problem in many tropical countries and the cause of 4-5 million deaths throughout the world annually1,2. Children are more susceptible to this disease which is the second leading cause of death of children under 5 years old3. Diarrhoea results from an imbalance between the absorptive and secretory mechanism in the intestinal tract accompanied by intestinal hurry, resulting in an excess loss of fluid in the faeces4. Diarrhoea is characterized as rapid movement of faecal matter through intestine resulting in poor absorption of water, nutritive elements and electrolytes producing abnormal frequent evacuation of watery stools. According to world health organization, it is the one of the most common cause of morbidity and mortality in many developing countries affecting mainly the infants and children5. It is often caused by enterotoxins which are produced by bacteria such as Escherichia coli, Salmonella typhi, Salmonella typhimurium, Clostridium difficile, Clostridium freundii, Aeromonas hydrophila, Campylobacter jejuni and Vibrio cholera to name a few. These bacteria cause the influx of water and ions to the intestinal lumen and thus increase the intestinal motility, thereby causing watery stools. Such secretory diarrhoea is treated by the administration of oral rehydration salts in children or adults to reduce the loss of essential electrolytes and maintain the body fluids osmolality6. The major causative agents of diarrhoea in humans include Shigella flexneri, Staphylococcus aureus, Escherichia coli, Salmonella typhi and Candida albicans7,8. Alternatively, many opiod drugs like Diphenoxylate, Loperamide, Diloxanidefuroate for protozoal infections induced diarrhoea and dysentery, racecadotril, muscarinic receptor blockers like atropine sulphate etc; are available in the market for treating diarrhoea. But all of the existing drugs suffer from adverse effects like the induction of bronchospasm, vomiting by racecadotril; intestinal obstruction and constipation by loperamide9. Combination of antidiarrhoeal drugs with different mechanisms of action are often used for synergistic action. The value of these combination have not been studied experimentally10. Capparisis a genus of about 850 species of woody trees, shrubs, vines, epiphytes, and hemi epiphytes in the family Moraceae. Capparis zeylanica is an umbrageous tree 9-12 meters having young branches at first, softly pubescent and afterwards glabrous. Flowering and fruiting period is from December-January. It is mostly found in dry and moist deciduous forest areas in South India. It is found mainly in Andhra Pradesh, Kerala, and Coimbatore, Dundigal, Namkkal, Niligiri, Salem, Theni, Tirunalveli and Vellore districts of Tamil Nadu state in India. The fruit is used as cardiotonic. The bark and leaves are used in liver and skin diseases. Bark is used in folklore practise11 for the treatment of cancer and hyperlipidemia. The leaf juice has antidysenteric activity. Roots possess antispasmodic activity. The leaves are reported to show antihyperglycemic12, gastroprotective13, invitro antioxidant14, antimicrobial, antihyperlipidemic15 activity. Inspite of all these pharmacological activities documented on the plant, antidiarrheaol activity has not been reported.

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Article

DEVELOPMENT, *IN-VITRO AND EX-VIVO* EVALUATION OF MUCO-ADHESIVE BUCCAL TABLETS OF HYDRALAZINE HYDROCHLORIDE

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Hydralazine hydrochloride is an anti-hypertensive drug. The drug has poor oral bioavailability (BA) of about 30- 50% due to extensive first-pass metabolism. Hence, the buccal delivery was used to enhance the BA of hydralazine hydrochloride. Buccal muco-adhesive tablets were prepared by direct compression technique, using carbopol 934P, HPMC K_4M, sodium alginate and sodium carboxy methyl cellulose (NaCMC) as muco-adhesive polymers. Prepared formulations were evaluated for physico-chemical characterization, *ex-vivo* residence time and *in-vitro* release studies. The some of the parameters viz hardness, thickness, weight variation are showing the values within the pharmacopeial limits. However, the swelling and bio-adhesive strength were increased with increasing polymer concentrations. From the *in-vitro* release studies, F9 buccal tablets prepared with NaCMC exhibited better release (96.56%, 6 h) profile than all other formulations and considerd as optimized. The release mechanism from kinetic methods suggests that, the drug release follows zero-order kinetics with diffusion mechanism. Thus, the buccal tablets of hydralazine hydrochloride showed enhanced BA and were further confirmed by *in-vivo* studies.

Key Words: Hydralazine hydrochloride. First-pass metabolism. Buccal muco-adhesive tablets. *In-vitro, ex-vivo.*

INTRODUCTION

Oral route is most preferred and widely applicable route for the delivery of majority of the drugs. But the problems such as poor aqueous solubility, less residence time, chemical instability in the gastrointestinal tract minimize the bioavailability (BA) of orally administered drugs (Dudhipala, Veerabrahma, 2016). Further, metabolism through various barriers or enzymes also degrades the drug before reaching site of action. Hence, various alternative drug delivery systems are developed to enhance the oral BA of these drugs. The delivery systems include; enhancement of solubility through solid dispersions (Ettireeddy *et al.*, 2017), complexation with cyclodextrins (Palem *et al.*, 2016a), liquisolid compacts (Arun *et al.*, 2018), increase the stability and prolonged residence time through floating systems (Dudhipala *et al.*, 2011; Senjoti *et al.*, 2016; Dudhipala *et al.*, 2016), increase the mucoadhesive property (Bomma *et al.*, 2014); lipid based delivery systems for by passing metabolism with solid lipid nanaoparticles (Dudhipala, Veerabrahma, 2015), transfersomes (Pitta *et al.*, 2018), nanostructured lipid carriers (Dudhipala *et al.*, 2018) and micronization for reducing particle size using nanosuspensions (Nagaraj *et al.*, 2017; Butreddy *et al.*, 2015).

The oral cavity is easily accessible for self-medication and is well accepted by patients. In the last three decades, there is a great interest in the research of buccal drug delivery system (Senel, Hincal, 2001). The

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METHOD DEVELOPMENT AND VALIDATION FOR THE SIMULTANEOUS ESTIMATION OF SOFOSBUVIR AND DACLATASVIR IN BULK AND TABLET DOSAGE FORM BY USING RP-HPLC IN BIORELEVANT DISSOLUTION MEDIA

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ABSTRACT

This study aimed to develop sofosbuvir and daclatasvir acid marketed formulation and to develop a stability-indicating HPLC method for their simultaneous estimation of sofosbuvir and daclatasvir acid in pure forms and in its final dosage forms in bio relevant media as per ICH guidelines. An isocratic mode HPLC method was performed; the flow rate was 1.0 ml/min, injected volume 10µL, and the mobile phases consisted of 50% phosphate buffer 3 pH and 50% acetonitrile, and UV detection was carried out at 238nm. Sofosbuvir and daclatasvir acid and their combined dosage form were exposed to thermal, oxidative, and acid-base hydrolytic stress conditions and the stressed samples were analyzed. The method's linearity, precision, accuracy, system appropriateness, and robustness were all validated. The method utilized is specific for estimating sofosbuvir and daclatasvir acid in the presence of degradation products and contaminants. The method was linear over the range of 80-400 µg/mL and 20-100µg/mL for sofosbuvir and daclatasvir acid, respectively. The mean recoveries for the accuracy studies were found to be within limits for sofosbuvir and daclatasvir acid, respectively. The per cent of standard deviation value (% RSD) was discovered to be less than the critical value. Our devised analytical approach is a stability-indicating, cost-effective, and relevant method that can be used to control the quality of sofosbuvir and daclatasvir acid in medicinal tablet formulations.

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Assessment of Oral Hygiene Complications and Status in Orthodontic Patients: A Prospective Observational Study

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Abstract: *This prospective observational study was carried out at Sai Ganesh Multi Speciality Dental Hospital in Naimnagar, Hanamakonda, spanning a 6-month period. The study aimed to assess oral hygiene complications and status in orthodontic patients, identifying factors contributing to poor oral hygiene. Findings revealed a prevalence of gingival bleeding and high plaque scores in patients with high sugar consumption, infrequent or improper brushing, and low usage of cleaning aids. Plaque index scores were determined using the teeth whitening shade guide and plaque control record, indicating a correlation between high plaque scores and gingival bleeding. The study underscores the suboptimal oral hygiene status among orthodontic patients and emphasizes the necessity of patient education to enhance oral hygiene practices and prevent potential orthodontic complications.*

Keywords: Orthodontic patients, Oral hygiene complications, Plaque score, Gingival bleed, Cleaning aids

1. Introduction

Oral hygiene is greatly complicated in orthodontic patients; the purpose of orthodontics is to place the tooth in a ideal occlusion. It functions by applying pressure to the tooth in order to gradually move in the desired direction. Depending upon the severity of the malocclusion, the condition of the tooth, gums and supporting bone and how strictly the patient was adheres to instructions, the length of time needed for braces differs from person to person. Some most common types of cleaning aids are dental flosses, inter-dental cleaners, mouth rinses, oral irrigates, rubber tip simulators and tongue cleaners .The complications include pain associated with orthodontic treatment and periodontal diseases.

2. Materials and Methods

Study Site: Sai Ganesh Multispecialist Dental Hospital, GMR & Complex, Naimnagar, Hanamakonda.

Study Type: Prospective observational study.

Study Period: Six months

Study Criteria:
Inclusion criteria: All age groups of orthodontic patients
Exclusion criteria: Except orthodontic patients other dental patients are excluded.

Source of Data: All the relevant data was collected through questionnaire form and it includes Teeth whitening shade guide; plaque control record and gingival bleed index

Forms included in the study
Questionnaire form
Teeth whitening shade guide Plaque control record Gingival bleed index

Study procedure
The study was conducted through direct interaction with patients. The patients teeth were examined through teeth whitening shade guide.

Responses were collected and their plaque score and gingival bleed score were analyzed.

Percent with plaque = The number of surface with plaque/number of tooth surface examined X 100

Low plaque score – 0-10%

Moderate plaque score – 10-20% High plaque score – more than 20%

Percent with gingival bleed = number of bleeding sites / total number of sites X 100 The data was collected throughout 6 months from 400 patients and analyzed. Total summarized data were collected and results are interpreted through graph pad prism.

3. Results and Discussion

Gender wise distribution

Gender	Total number of population
Male	190
Female	210

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Original Research Paper

Pharmacy

EVALUATION OF PREVALENCE AND RISK FACTORS OF HYPERTENSION IN SCHOOL CHILDREN

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ABSTRACT **Background:** Hypertension in children is defined as elevating blood pressure of both systolic and diastolic equal to or greater than 95th percentile by age, gender, height and weight. According to ESH (European society of hypertension) and AAP (American academy of pediatrics) an increasing trend has been observed in the incidence, prevalence of hypertension in children, this study is expected to improve awareness in people regarding hypertension in children. **Aim:** This study was performed to evaluate the incidence, prevalence and risk factors of hypertension among school age children and to assess relationship between physical activity of children with their blood pressure **Materials and Methods:** The study was a cross sectional observational study carried out at different schools in Hanam Konda. All the data were collected from the children by interacting with them directly by using data collection form and physical activity questionnaire. **Results:** Among the total sample population, subjects with hypertension were found to be 27. Among which females were 11(41%) and males were 16(59%). subjects with sedentary lifestyle were found to be 14 (52%) and 5(19%) subjects were found to be obese out of 5 members 4 members are having sedentary lifestyle, and 5(19%) subjects were found to have concomitant disease conditions and 3(38%0 were found to be with family history. **Conclusion:** This study suggests that hypertension in children is a considerable public health challenge worldwide. Childhood hypertension is rare in children but the occurrence of hypertension in children was common now a days due to family history, obesity, sedentary lifestyle and other disease conditions. According to our study we concluded that changing dietary habits, increasing physical activity in children and creating awareness regarding childhood hypertension in children and their parents may reduce the prevalence rate in children.

KEYWORDS : Nephrotic syndrome, obesity, hypertension, sedentary lifestyle

Introduction

Definition: Two standard guidelines are used for hypertension in children include ESH (European society of hypertension) guideline introduced in 2016 and AAP (American academy of pediatrics) guideline introduced in 2017. [Table 1] According to these recommendations, childhood hypertension is characterized by elevated systolic blood pressure and diastolic blood pressure that are equivalent to or higher than the 95th percentile by age, gender, and height at three or more visits. These recommendations define normal blood pressure as falling within or below the 90th percentile for one's age, gender, height, and weight. (3)

Table .1

CATEGORY/CLASS	SBP/DBP PERCENTILE
Normal	Less than 90th percentile
Prehypertension	Greater than 90th – less than 95th percentile
Hypertension stage 1	95th – 99th percentile
Hypertension stage 2	Greater than 99th percentile

Table .2 Screening BP Levels Needing Further Analysis

Years of age	Boys	Girls
	SBP/DBP (mmHg)	SBP / DBP (mmHg)
10 years	110/70	110/70
11 years	110/75	115/75
12 years	120/75	120/70
> 13 years	120/80	120/80

Epidemiology: Previous studies showed prevalence of hypertension in children is 2-3% and 9.02% urban & 17.47% in rural. Hypertension prevalence in children with type 1 diabetes mellitus is 4-16%, type 2 diabetes mellitus is 12-31%, neuro fibromatosis is 6.1% and chronic renal disease is 20-70%. The prevalence of HTN is also based on race and their food habits (2)

Risk Factors: Obesity, Gender, Family history, Sedentary lifestyle, Race. (4)

Etiology: Primary hypertension occurs without any exact cause or does not occur due to other medical conditions which are caused by low birth weight, prematurity, unhealthy dietary habits like high salt and calorie intake, obesity, family history, gender, type-2 diabetes mellitus, high cholesterol levels, sedentary lifestyle.

Secondary hypertension occurs due to exact cause and with other medical conditions include glomerulonephritis, renal vein thrombosis, hyperthyroidism, polycystic kidney disease, arterial venous fistula, William syndrome, thrombocytopenic purpurea, increased intracranial pressure, stroke, sleep disorders (obstructive sleep apnea), drugs include glucocorticoids, oral contraceptives, decongestants. (8)

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Drug Selection Patterns in Asthma and Hyperre Active Airway Disease in Children

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Abstract:- A prospective observational study was conducted at Mahatma Gandhi Memorial (MGM) hospital, Warangal over a period of 6 months. This study is conducted to evaluate clinical presentation of various respiratory conditions and to optimize oxygen, inhalational therapy and antibiotic treatment for optimal outcome. We conclude that many children were under 5 commonest age group, suffering from wheeze, respiratory distress and asthma. Nebulization of salbutamol was useful in HRAD and asthma rather than bronchiolitis and LRTI. IV hydrocortisone was beneficial in HRAD and less beneficial in bronchiolitis. Supplemental oxygen was most effective treatment in bronchiolitis condition. None of the children were receiving holding chambers or spacers. At least some percentage of the children in the present study may require spacers in long term use to decrease morbidity.

Keywords:- *ASTHMA, HRAD, LRTI, SABA, LABA, PRAM.*

I. INTRODUCTION

A. ASTHMA:

Asthma is a severe inflammatory disease, which is identified by audible wheezing in children, chest tightness, coughing (most seen at night time), shortness of breath, fever, cold and several airways obstruction. Asthma diagnosis is done based on patient history, physical examination and pulmonary function tests.

- **Risk factors:** Allergies related to food, Inhalation of dust particles and adulterants, Parental exposure to allergies, Rhinitis, Inhalation of secondary smoke, Eczema and dermatitis, Cool wind. Under diagnosis and under treatment is due to comorbid conditions such as upper respiratory tract infection (URTI) and weak condition of the body, different phenotypes, intermittent occurrences of coughing and wheezing, non-medication adherence, poor economic status and disease understanding of the patient, improper usage of inhaler and continuous exposure to allergic annoyances. (1)

➢ *TREATMENT:*

- **SUPPORTIVE THERAPY:**

Oxygen therapy- It is the most suitable and beneficial therapy for mild intermittent, persistent and severe asthma. Both warm and cold humidifiers are used for various improvement reasons from life-threatening conditions. There is no evidence from research side of using oxygen therapy in acute conditions.

✓ Asthma in pre-school-

It is difficult to diagnose asthma in pre-school children as they experience symptoms which are, most of the time related to viruses and lead to coryza. Advanced utilization appertaining to corticosteroids for patients progressed from 1 year to 12 years resulted in no fast breathing for over 7 days.

✓ LABA-

These are not commonly used because of the adverse effects. Salmeterol used only in repeated interventions of exacerbations and for exercise-related asthma. And it should be discontinued immediately after the child feels less discomfort. It is used together with ICS, alone can increase the chances of future asthma-attacks and increase mortality rate.

✓ Monoclonal antibodies-

Omalizumab is used with inhaled corticosteroids for its synergistic effect. However, it is not commonly prescribed as it may provide lesser obstruction of the airways.

✓ SABA and bronchodilators-

These are the drugs mainly used to reduce bronchospasm or shortness of breath associated with nightly awakenings. Based on a comparative study, it concludes the use of an inhaled form of salbutamol- 2 puffs has greater chances and quick response of immediate relaxation of airways were found compared with oral format of same drug. It will provide its action with accompanying relaxation effect on airways.

✓ Corticosteroids-

Prednisone is converted to prednisolone, an active metabolite in which its oral dose should be less than 20mg in children. Increasing the dose of the drug may lead to serious adverse events. It is metabolized by the liver. It lowers the inflammation of the airways of bronchioles. After achieving improvement with combination of LABA/ICS, discontinuation of LABA should be implicated and use of ICS should be continued.

✓ Magnesium sulphate (mgso4)-

It was originally used in the year 1906 by horn in seizure condition during gestation, then is used in asthma for relaxation of airways or hyperinflation. Its primary mode of action is blocking of calcium affluence which is used for muscle contraction and also cessation of histamine production such as bradykinins and cytokinin release from mastocyte.

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Review Article

Approaches to Improve Oral Bioavailability of Antihypertensive Drugs: A Mini-Review

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Abstract

Hypertension elevates the risk of heart disease and stroke which are one of the most frequent causes of death. Fortunately, hypertension is manageable with the use of anti-hypertensives and a healthy lifestyle. However, patient non-adherence to the prescribed dosing regimen is the primary reason for uncontrolled blood pressure levels. Daily multiple doses of medication are one of the major reasons for patient non-compliance to the dosing regimen. Multiple doses of medication are a result of low solubility and high first-pass metabolism of anti-hypertensives. There are several approaches to improve the bioavailability of anti-hypertensives like polymeric and non-polymeric approaches to enhance solubility, avoiding first-pass metabolism through alternate routes of drug delivery and others. The objective of this review is to discuss different approaches to enhance the oral bioavailability of anti-hypertensive drugs.

Keywords: Solubility enhancements, solid lipid nanoparticles, hot melt extrusion, drug delivery, pharmacokinetics, poorly soluble, oral bioavailability.

Introduction

Hypertension is a cardiovascular disease (CVD) resulting in increased blood pressure. As per the Centers for Disease Control and Prevention, there were 670,000 hypertension-associated deaths in the United States in 2020. WHO estimates that there are 1.28 billion adults who are suffering from hypertension. Hypertension is prevalent in countries with low and middle income compared to high-income countries. As per WHO (Geneva) report in 2008, hypertension caused about 45% of deaths due to ischemic coronary illness and 51% of death as a result of stroke. In 1980, 600 million individuals were experiencing hypertension, while in 2008 this figure increased to 1 billion raising a major concern for its management (WHO, 2013)[1-7].

The risk of hypertension increases drastically after 45 years. For a forty-five-year-old without hypertension, the risk of developing hypertension in the next 40 years is 93% for African Americans, 92% for Hispanics, 86% for whites, and 84% for Chinese adults. Hypertension was the prominent reason for death and adjusted life due to disability in 2010. Hypertension had more impact on women compared to men and African Americans in comparison to whites. The risk of cardiovascular diseases increases in a log-linear fashion with an increase in systolic blood pressure (SBP) levels from 115-180 mm of Hg and an increase in diastolic blood pressure (DBP) from 75-105 mm of Hg. A 20 mm Hg increase in SBP and a 10 mm Hg increase in DBP are associated with a doubling in the risk of death due to stroke, heart disease, or other vascular disease. In persons higher than 30 years of age, higher SBP and DBP are linked with increased risk for CVD, angina, myocardial infarction (MI), heart failure (HF), stroke, peripheral arterial disease, and abdominal aortic aneurysm[8-9].

The anti-hypertensive drugs that are now on the market may be divided into each of the following groups:

A. Diuretics

a) Thiazides

b) High ceiling

c) Potassium sparing

B. Renin angiotensin system inhibitors

a) ACE inhibitors

b) Angiotensin (AT1) receptor blockers

c) Direct renin inhibitors

C. sympathetic inhibitors

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CHOLELITHIASIS- A REVIEW

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Abstract: Cholelithiasis, or gallstone disease, is the presence of gallstones in the biliary tract. More specifically, cholecystolithiasis describes gallstones present in the gall bladder and can lead to cholecystitis, whereas choledocholithiasis describes gallstones present in the common bile duct and can lead to ascending cholangitis. It is more prevalent in developed countries, particularly among individuals of western descent, and its incidence increases with age. Women are more susceptible to gallstone formation compared to men, with hormonal factors playing a significant role. The clinical presentation often depends on the location and size of the gallstones and whether they cause any obstruction or inflammation in the biliary system. Management of gallstones can be divided into two categories asymptomatic gallstones and symptomatic gallstones. Preventing gallstone formation and associated complications is possible through various lifestyle modifications and risk factor management.

Index Terms **- Gallstones, Biliary Colic, Cholecystectomy, Inflammation.**

I. INTRODUCTION

Cholelithiasis, commonly known as gallstone disease, is a medical condition that affects millions of individuals worldwide. It is a prevalent and clinically significant gastrointestinal disorder, refers to the formation of solid crystalline deposits, known as gallstones, within the gallbladder or bile ducts. These stones formed are mainly composed of two substances: cholesterol and calcium bilirubinate. This condition has substantial implications for public health due to its association with various complications, including biliary colic, acute cholecystitis, and choledocholithiasis. Choledocholithiasis develops in about 15% of patients with cholelithiasis occurs due to the migration of stones from the gall bladder into the bile ducts[1].Understanding the pathogenesis, risk factors, diagnostic modalities, and evolving management strategies for cholelithiasis is imperative for clinicians and researchers alike.

Gallstones, also referred to as choleliths, are solid deposits that can vary in size and composition. They are predominantly composed of cholesterol, bilirubin, and calcium salts, although the exact composition may differ among individuals. Gallstones can form in various parts of the biliary system, including the gallbladder, common bile duct, and hepatic ducts. The presence of these stones can lead to a wide spectrum of clinical manifestations, ranging from asymptomatic gallstones to acute cholecystitis, obstructive jaundice, and pancreatitis. In patients with asymptomatic gall stones discovered incidentally, the likelihood of developing symptoms or complications is 1 to 2% per year[2].

II. EPIDEMIOLOGY:

Cholelithiasis is a common gastrointestinal disorder, and its prevalence varies across different populations and regions with an overall prevalence rate of 2 – 29%[3]. It is more prevalent in developed countries, particularly among individuals of western descent, and its incidence increases with age. Women are more susceptible to gallstone formation compared to men, with hormonal factors playing a significant role. Prevalence is low in Asian population with a female to male ratio of 3:1[4]. The prevalence of gallstones also tends to increase during pregnancy and with certain medical conditions such as obesity and metabolic syndrome. Some epidemiological studies using ultrasound examination have determined the factors favouring lithogenesis in addition to which are already well known such as age, obesity, female gender, high blood triglyceride levels and multiparity, the risk is correlated with high frequent variations in weight, intake of certain drugs and with their sedentary lifestyle habits[5]. Gallbladder disease is generally considered uncommon in childhood, but the frequency seems to be increasing in recent years[6].

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Viral Hepatitis – A Review Article

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Abstract

Hepatitis is inflammation of the liver that can result from a variety of causes such as alcohol overconsumption, autoimmune, medications, or toxins.Hepatitis can be further classified into acute and chronic. If inflammation of the liver lasting for less than 6 months, is termed as acute hepatitis and greater than 6 months is termed as chronic hepatitis.Hepatitis is a significant public health issue in developing countries, having varying morbidity and mortality rates.Hepatitis A and E infections are typically self – limiting and do not result in chronic liver disease, but can cause significant morbidity and mortality in people with underlying liver disease. Hepatitis B is a major global health issue, about 257 million people are living with chronic hepatitis B infection. Hepatitis D is relatively rare and usually infect people who are already infected with hepatitis B. Clinical pharmacist can play a major role in reducing the spread of infection by properly educating the patient about spread of disease and hygiene.

Keywords: Hepatitis, Liver, Morbidity, Mortality, Clinical Pharmacist

Introduction

Viral hepatitis has been a redoubtable challenge, with proved outbreaks 5000 years ago in China and analogous jaundice descriptions by Hippocrates in the 5th century BC in the Island of Thassos[1]. Hepatitis is inflammation of the liver that can result from a variety of causes such as alcohol overconsumption, autoimmune, medications, or toxins. Viral infection is the most frequent cause of hepatitis. Hepatitis A,B and C are most common types of hepatitis whereas hepatitis D and hepatitis E are less commonly encountered[2].Hepatitis B and D are the most chronic types of Hepatitis and leads to Liver cirrhosis and Liver Cancer, and are responsible for a significant number of deaths each year.The severity of hepatitis can range from mild and self-limiting to severe illness requiring liver transplantation based on causative factor. Based on the duration of the inflammation, Hepatitis can be further classified into acute and chronic[3].If inflammation of the liver lasting for less than 6 months, is termed as acute hepatitis and greater than 6 months is termed as chronic hepatitis. Acute hepatitis is usually self-resolving but it can cause fulminant liver failure based on the etiology. Whereas, chronic hepatitis can cause liver damage that includes hepatocellular carcinoma,liver fibrosis, cirrhosis, and features of portal hypertension leading to significant morbidity and mortality[4].

Epidemiology

Millions of people Worldwide are getting affected by Hepatitis and it is a global health issue.Hepatitis is a significant public health issue in developing countries, having varying morbidity and mortality

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RESEARCH ARTICLE

OPEN ACCESS

DEPRESSION AND ANXIETY DISORDERS IN THYROID PATIENTS

Gunisetti Tejaswini, Muta Apoorva, Thokala Manisha, Namilikonda Rachana, Ravi Chander Thatipelli and Tejaswi Chillara*

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Thyroid, Anxiety, Depression, Hamilton scale.

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ABSTRACT

This study was done to assess medication adherence, awareness in thyroid patients and to evaluate the depression and anxiety in thyroid patients using depression and anxiety scales. A randomised observational study was conducted in the primary health care centres and through direct visits to homes in Hanamkonda for a period of 6 months. In the overall study we collected 406 thyroid patients' data in this 305 were hypothyroidism and 101 were hyperthyroidism. The total data was analysed using the scoring system to find out the ranges. From our study we concluded that thyroid conditions would affect the mental health condition of the person.

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INTRODUCTION

The thyroid is a butterfly-shaped gland, is situated immediately below the larynx. It produces hormones that regulate the body's energy consumption. These hormones have an impact on every organ in our body and regulates a number of the most vital processes.

Secretion: Thyroid hormone synthesis and release are stimulated by thyroid-stimulating hormone (TSH) from the anterior pituitary and thyrotropin-releasing hormone (TRH) from the hypothalamus [12].

Functions: Increase baseline metabolic rate, promote protein synthesis, improve excretion of cholesterol, hasten the growth of the body, and promote nervous system development.

Synthesis: Thyroid follicular cells actively move iodide ions (I-) from the circulation into the cytosol. Thyroglobulin (TGB), a large glycoprotein made by the follicular cells involving in capturing (I-) TGB will undergo iodization $I^- \rightarrow I2$. Mono- iodotyrosine (T1) is produced when one iodine atom is bounded, and diiodotyrosine is formed when two ionizations occur (T2). Either one T1 and one T2 molecule or two T2 molecules combine to generate T4. TGB is broken down by digestive enzymes in the lysosomes, which release molecules of T3 and T4. T3 and T4 diffuse through the plasma membrane into interstitial fluid and subsequently into the circulation.

Although T4 is often secreted in greater amounts than T3, T3 has a far higher potency. Additionally, the majority of the T4 that enters a body cell is converted to T3 by removing one iodine.

Types of thyroid disorder: Hypothyroidism, Hyperthyroidism.

Hypothyroidism: Insufficient thyroxine (T4) production or secretion by the thyroid gland results in hypothyroidism.

Hyperthyroidism: increased thyroid hormone synthesis, excessive release of thyroid hormones, an abnormal concentration of thyroid hormones in the tissues, known as hyperthyroidism [8].

Thyroid hormone metabolism in the brain: Thyroid function issues can have a major impact on mental status, including emotion and cognition. Both too much and too enough thyroid hormones can lead to mood disorders, including depression, which is typically curable with effective thyroid medication.

Psychiatric manifestations of thyroid disorders: The neuropsychiatric symptoms of primary thyroid diseases, such as hypothyroidism and hyperthyroidism, can range from mild anxiety and depression to overt psychosis [12].

Need for the study: The study is to assess mental illness, knowledge, and dietary changes in hypothyroidism and hyperthyroidism patients and to educate the patients regarding thyroid problems, their complications, and the advantage of medication adherence.

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Open Access to Pharmaceutical and Medical Research

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Review Article

Approaches to Improve Oral Bioavailability of Antihypertensive Drugs: A Mini-Review

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The risk of hypertension increases drastically after 45 years. For a forty-five-year-old without hypertension, the risk of developing hypertension in the next 40 years is 93% for African Americans, 92% for Hispanics, 86% for whites, and 84% for Chinese adults. Hypertension was the prominent reason for death and adjusted life due to disability in 2010. Hypertension had more impact on women compared to men and African Americans in comparison to whites. The risk of cardiovascular diseases increases in a log-linear fashion with an increase in systolic blood pressure (SBP) levels from 115-180 mm of Hg and an increase in diastolic blood pressure (DBP) from 75-105 mm of Hg. A 20 mm Hg increase in SBP and a 10 mm Hg increase in DBP are associated with a doubling in the risk of death due to stroke, heart disease, or other vascular disease. In persons higher than 30 years of age, higher SBP and DBP are linked with increased risk for CVD, angina, myocardial infarction (MI), heart failure (HF), stroke, peripheral arterial disease, and abdominal aortic aneurysm[8-9].

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c) Direct renin inhibitors

C. sympathetic inhibitors

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A Prospective Observational Study on Causes and Effectiveness of Oligohydramnios Treatment in Pregnant Women with Different Comorbidities

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Original Research Article

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ABSTRACT

Oligohydramnios is a rare condition characterised by decreased amniotic fluid volume for gestational age. To determine the causes and effectiveness of oligohydramnios treatment in oligohydramnios pregnant women. We conducted a prospective and observational study at GMH (Government Maternity Hospital) in Hanamkonda over a period of 6 months. We included 203 oligo patients in this study and in which patients were grouped as 3 categories based on amniotic fluid index (AFI) as mild, moderate, severe. Information of the patients were collected from patient case reports and face to face interactions. The data was analysed through EXCEL. From our study we

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A Prospective Observational Study on Causes and Effectiveness of Oligohydramnios Treatment in Pregnant Women with Different Comorbidities

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ABSTRACT

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Medication Adherence in Renal Patients

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Original Research Article

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ABSTRACT

Background: Medication adherence is defined as extent of patients taking medications as prescribed by doctors. It is the major factor that determines the therapeutic outcomes in the patient. Non adherence is quite common problem in most of the patients which is dangerous and can increase treatment expenses.
Aims: The study was conducted to evaluate and identify various reasons leading to non-adherence which can result in unpleasant consequences in the renal patients.
Materials and Methods: The study was a prospective observational study that was performed through a questionnaire for 6 months. The data collected includes renal patient's demographic details, past history, complaints, medications and interviewed them regarding their medications use by using morisky adherence questionnaire.
Results: The study was performed on 300 renal patients in the nephrology department. From this data around 31(10%) of the patients were completely adherent and 269(90%) of the patients were non-adherent to the medications. 66(24%) were non-adherent due to forgetfulness about medications, 49(18.2%) were non-adherent because of very frequent changes made in the drug regimen, 63(23.4%) of the patients were non-adherent because of expensive medicines.

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FORMULATION & EVALUATION OF HERBAL LIPSTICK FROM CITRULLUS LANATUS & CURCUMA LONGA

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ABSTRACT:

In current running technology cosmetics has high demand in the market with fewer side-effects. Herbal cosmetics has eco-friendly nature substance with causes lesser adverse effects. At present herbal cosmetics are the trending in fashions. Most of the herbal cosmetics are nature-based cosmetics. Lipstick is an herbal cosmetic which contains pigments, oils, waxes which protect and applies colour and texture to the lips. Lipstick is a general cosmetic that is worn by women. The current work is aimed to prepare an herbal lipstick from colour pigments of *curcuma longa* and *Citrullus lanatus* and the preparation consists of ingredients such as olive oil, bees wax, white soft paraffin, acacia, coloured pigment of *curcuma longa, & Citrullus lanatus,* strawberry, lemon juice & vanilla essence. Due high side effects of the chemicals, natural products are used for the formulation. The prepared formulation is evaluated for various parameters such as P^H, melting point, skin irritation test, solubility test, breaking point etc. were performed for safe and effective use of the formulation.

Keywords: Curcuma longa, Citrullus lanatus, lipstick, herbal, cosmetics, pigment Eco-friendly.

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INTRODUCTION:

Lipstick is one of the decorative cosmetic products that command a unique market segment. Lipsticks are the common colour cosmetics used by women in their daily life. The essential factors are pleasant colour, safety, smell, luster, stability, adhesion & extensibility. Usually, customers are concerned more about the feel, colour & lasting effects of lipstick. It has been used for many years to impart colour to the lips. The colour helps to define the mouth area while imparting cosmetic shades that are suitable with fashion trends. The vast range of colours of lipsticks are derived from edible pigments. Every year, users are introduced with various new cosmetic products of the latest trend. Lipsticks contain a variety of emulsifiers, preservatives, emollients, colorants &binders. The previous research proves that the quality of lipstick is directly linked to the basic materials that used in the formulation by varying the ratio of the ingredient in formulation, the final product characteristics such as viscosity, melting point, texture & hardness of the lipstick can be specified

PLANT PROFILE

CITRULLUS LANATUS (WATERMELON):

Watermelon is a flowering plant species of the Cucurbitaceous family and the name of its edible fruit. It requires a long growing season in the subtropics, but fast growing in the tropical regions. Flowering and fruit development are promoted by high light intensity and high temperature.

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FORMULATION AND EVALUATE SUBLINGUAL TABLETS OF LOSARTAN POTASSIUM USING DIFFERENT SUPERDISINTEGRANTS

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ABSTRACT

The concept of sublingual tablets containing Losartan potassium offers a suitable and practical approach to serving the desired hypertension management objective. Most of the excipients used in the formulation are water-soluble and hence have better patient acceptability. The present work of formulating a sublingual tablet containing Losartan potassium successfully reduced manufacturing difficulties, improved patient compliance with effective medication, and overcame. It has been observed from the above study that excipients like mannitol, microcrystalline cellulose, sodium starch glycolate, and flavor orange were found to be ideal excipients and effective for formulating sublingual tablets. Sublingual tablets provide several advantages, especially for children and elderly patients. In addition, rapid absorption into the systemic circulation may be achieved within a short period. The sublingual tablets of Formulation F3 contained 25 mg of Losartan Potassium, 46 mg of MCC PH 102, 20 mg of mannitol (DC), crospovidone 6mg, talc 1mg, magnesium stearate 1mg, and aspartame was considered to be the best among all other nine batches of tablets since it exhibited an excellent dissolution profile, disintegration time, appearance, uniformity of drug content.

Keywords: Losartan, Sublingualtablets, Medication, Dissolutionprofile, Mannitol

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1.INTRODUCTION

Developing a formulation involves much study and experimental work to get optimum results. While doing so, we mustconsider various factors, such asthe choice of excipients, drug bioavailability, drug stability in required dosage

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Mallory-Weiss Syndrome: A Case Report

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Abstract

Mallory Weiss Syndrome (MWS) manifests as a tear in the mucous membrane or inner lining of esophagus-to-stomach junction. Most tears recover naturally in 7–10 days, although MWS might result in considerable bleeding. Severe or protracted vomiting is the most typical cause of MWS. While this kind of vomiting can also be brought on by stomach ailments, it also happens in prolonged alcoholism or blumia. In the majority of cases, the symptoms will manifest as bloody or black stools, hematemesis, involuntary retching, and stomach pain. The red blood cell count may be low as a result of esophageal bleeding if symptoms point to active bleeding, which the doctor would diagnose with an esophagogastroduodenoscopy (EGD).The National Organisation for Rare Disorders estimates that in roughly 80–90% of MWS cases, the bleeding caused by esophageal tears will stop on its own. If bleeding persists, coagulation therapy and sclerotherapy are the preferred treatments. Famotidine and lansoprazole are used to lessen the production of stomach acid.

Keywords: Mallory weiss syndrome, coagulation therapy, sclerotherapy, Famotidine, lansoprazole

Introduction

One of the frequent causes of acute upper gastrointestinal bleeding is Mallory-Weiss syndrome, which is characterized by longitudinal superficial mucosal lacerations (Mallory-Weiss tears). These tears primarily affect the gastroesophageal junction, although they can also spread distally to affect the stomach's proximal part or lower to middle esophagus.

• Although Kenneth Mallory and Soma Weiss more accurately described this condition as lower esophageal lacerations (not ulcerations) happening to patients with repetitive forceful retching and vomiting after excessive alcohol intake in 1929, Albers first described lower esophageal ulceration in 1833.

• Severe or protracted vomiting is the most typical cause of MWS. This kind of vomiting can happen when one has a gastrointestinal sickness, but it also happens regularly as a result of bulimia or prolonged alcohol consumption.

• In mild circumstances, the illness can not show any symptoms.

• Hematemesis is the first symptom to appear in 85% of cases.

• Melena, lightheadedness, or syncope are additional symptoms that may appear in cases of significant bleeding. The existence of a predisposing gastroesophageal reflux disease (GERD), which is indicated by presence of epigastric pain.

Risk Factors: Heavy alcohol consumption, Bulimia nervosa diagnosis, chronic acid reflux and extreme vomiting.

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INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

A PROSPECTIVE OBSERVATIONAL STUDY ON DRUG UTILIZATION REVIEW OF DMARD'S IN TERTIARY CARE RHEUMATOLOGY CENTRE

Pharmaceutical Science

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ABSTRACT

This study was conducted to determine the percentage evaluation of DMARDs and to evaluate the most pharmacoeconomic drug. This study was carried out in Dr NARESH ARTHRITIS & RHEUMATISM CENTRE, Hanamkonda for a period of 6 months. From our study we can conclude that percentage utilization of DMARDS was found to be (94.90%) which is considered to be higher among other categories of drugs. methotrexate is considered as an affordable drug among other DMARDs.

KEYWORDS

Drug utilization review, DMARDs, Rheumatoid arthritis, Methotrexate.

INTRODUCTION:

Drug Utilization Review:

Drug utilization review is an authorized, structured, ongoing review of prescribing, dispensing & use of medication. It ensures proper medication decision-making & positive outcomes. It is classified into 3 types:

Prospective
Retrospective
Concurrent

IMPORTANCE OF DUR:

It plays an essential role in helping the healthcare systems to improve prescribing, administration & use of medications. DUR results are used to encourage more efficient use of limited health care resources. It provides an opportunity for pharmacists to identify trends in prescribing medications. DURs are used as tools in health economics.

RHEUMATOLOGY DEPARTMENT:

Rheumatology is a field of medicine that deals with the diagnosis and treatment of rheumatic diseases.

Ex: Autoimmune diseases (Rheumatoid arthritis, Psoriatic arthritis, SLE) Autoinflammatory diseases (Behcet's disease, familial Mediterranean fever) Vasculitis

DISEASE MODIFYING ANTI-RHEUMATIC DRUGS (DMARDs) THERAPY:

Rheumatoid arthritis patients are prescribed with a group of medications known as DMARDs.

DMARDs act by suppressing the body's overactive immune system or the underlying inflammatory condition.

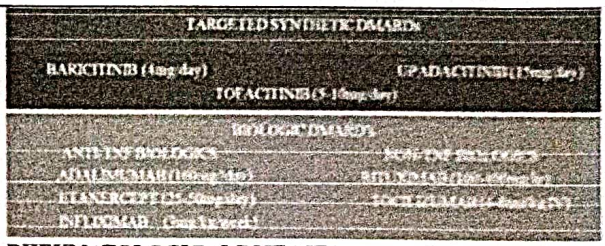
DMARDs are usually used in union with NSAIDs & CORTICOSTEROIDS to prevent further joint destruction

OPTING BETWEEN DMARDs:

The choice of DMARDs is considered depending on Stage and seriousness of patient's condition.
Balance between risk and benefit.
Economic status.

TYPES OF DMARDs:

DMARDs differ greatly in their production, cost, administration, and side effects.



RHEUMATOLOGICAL DISEASES:

RHEUMATOID ARTHRITIS:

Rheumatoid arthritis is an autoimmune disease when a person's immune system mistakenly attacks the normal proteins within the body. The resulting chronic inflammation primarily affects the synovium (the lining of the joints), leading to swelling, stiffness, pain & deformation of joints.

PSORIASIS:

Psoriasis is an auto-immune disease, causing inflammation in the body. It is a complication of psoriasis. The common signs such as plaques & scales on the skin are visible. It results in increased skin cell growth because of an overactive immune system.

GOUT:

Gout is an inflammatory disease in which monosodium urate crystals deposit into a joint, making it red, hot, tender, & swollen within hours. When it occurs, called as gouty attack.

OSTEOPOROSIS:

Osteoporosis is a result of the demineralization of bones leading to low bone mass, fragility of bones and porous bones thereby increases the risk of fractures. It can occur as a result of an imbalance between resorption & the bone formation rate.

OSTEOARTHRITIS:

Osteoarthritis is a medical syndrome characterized by arthralgia & dysfunction of articular cartilage due to joint degeneration. It occurs due to wearing down of protective cartilage cushioning the joints, which leads to structural issues in the joint.

FIBROMYALGIA:

Fibromyalgia is a condition that causes myalgia associated with tenderness, sleep issues, tiredness, & cognition impairment. It is not a life-threatening condition but affects the quality of life. The pain can be burning, aching, throbbing, tingling, stabbing, or numbing in onset.

SYSTEMIC LUPUS ERYTHEMATOSUS:

It is a chronic autoimmune disease involving multi-system inflammation. The disease has a relapsing and remitting course. It involves the production of autoantibodies against the body's immune system leading to the formation of the immune complexes which get deposited into the various areas of the body.

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A PROSPECTIVE OBSERVATIONAL STUDY ON EPIDEMIOLOGICAL EVIDENCE AND PRESCRIPTION PATTERN IN RHEUMATOID ARTHRITIS AND OSTEOARTHRITIS

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ABSTRACT

Background: Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease of multiple joints, and Osteoarthritis (OA) is progressive degenerative condition of joints. An increasing trend has been observed in the incidence and prevalence of RA and OA, and by analysing the Drug usage pattern among RA and OA patients, this study is expected to improve awareness of Rational prescribing. Proper adherence to medication is crucial for improved outcomes in RA. **Aims**: This study was performed to determine the prevalence, incidence, and drug prescribing patterns in RA and OA patients and to assess the medication adherence in RA patients. **Materials and Methods**: A Prospective Observational study was carried out at Naresh Arthritis and Rheumatism Centre, Hanamkonda, for six months. The data collection form consists of the patient demographic details, treatment charts and MMAS-8 scale. **Results**: Among the total study population of 603 patients with RA and OA, 504 (84%) and 99 (16%) were diagnosed with RA and OA respectively. The prevalence of both RA and OA was highest in females than in males. The commonly prescribed drug classes in RA were DMARDS (100%), NSAIDS (86.66%), CORTICOSTEROIDS (80.5%), VITAMIN SUPPLEMENTS (80%) while in OA were NSAIDS (86%), VIT-D3 AND CALCIUM SUPPLEMENTS (19.34%), and OPIOID ANALGESICS (14%). In RA, 75% of patients were non-adherent to their medication. **Conclusion:** There was a significantly higher disease prevalence of RA (3:1) and OA (1.3:1) in women than in men. The mostly prescribed drug categories were DMARDS and NSAIDS, respectively. Significantly low medication adherence (75%) was found in RA.

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RESEARCH ARTICLE

Dehydrozingerone promotes healing of diabetic foot ulcers: a molecular insight

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Abstract

Introduction One of the most common problems of diabetes are diabetic foot ulcers (DFUs). According to National Institute for Health, initial management of DFUs can decrease the complication of limb amputations and can improve the patient's quality of life. DFU treatment can be optimized with the help of multidisciplinary approach. Based on many studies, control of glucose levels in blood, antioxidant activity, reduction in cytokine levels, re-epithelialization, collagen formation, migration of fibroblasts are major phases involved in managing DFU. Dehydrozingerone (DHZ), has been known for its anti-inflammatory, antioxidant and wound healing properties.

Methodology Three months high-fat diet and low dose of streptozotocin-induced type-II diabetic foot ulcer model was used to evaluate the effectiveness of dehydrozingerone. DHZ was given orally to rats for 15 days post wounding. TNF-α, IL-1β and antioxidant parameters like lipid peroxidation, glutathione reductase were estimated. Immunoblotting was done to investigate the effect of DHZ on the expression of ERK, JNK, HSP-27, P38, SIRT-1, NFκB, SMA, VEGF and MMP-9 in skin tissue. Histopathology was performed for analyzing DHZ effect on migration of fibroblasts, formation of epithelium, granulation tissue formation, angiogenesis and collagen formation.

Results DHZ decreased the levels of malondialdehyde, TNF-α, IL-1β and increased glutathione levels in wound tissue. Western blotting results suggested that DHZ activated ERK1/2/JNK/p38 signaling, increased expression of HSP-27, SIRT-1, VEGF, SMA thus facilitating the migration and proliferation of fibroblasts, angiogenesis and decreased inflammation. Masson Trichrome & histopathology showed an increase in collagen, epithelial and granulation tissue formation.

Conclusion DHZ significantly accelerates the healing of diabetic foot ulcers in high fat diet fed plus low dose streptozotocin induced type-II diabetic Wistar rats.

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Notch signaling: A possible therapeutic target and its role in diabetic foot ulcers

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ABSTRACT

Background & aim: Diabetic foot ulcers are major cause of lower limb amputations in the diabetic population. The major factors that play a role in causing the delay of the process of healing in diabetic foot ulcers broadly are decreased angiogenesis, reduced proliferation and migration of keratinocytes/fibroblasts. The typical wound healing process has four phases which are overlapping with each other thus making the healing even more complex. Hence it is essential to identify a therapeutic target that involves the regulation of the cellular factors involved in healing and helps to increase angiogenesis and can regulate all four phases accordingly.

Method: Literature review involved a search of the databases namely, PubMed, Cochrane, EMBASE, and Web of Science database. Articles were identified and retrieved that specifically dealt with Notch as a target in healing of wounds and its mechanism of action on various cells and phases of healing.

Results: Notch is a cell surface receptor which interacts with transmembrane ligands of the nearby cells and is involved in cell proliferation, differentiation, cell fate and death. It is also involved in cell-to-cell communication, cell signaling, and various phases of development. There exist four known notch genes and five ligands which interact with notch proteins. Hyperglycemia plays a role in the activation of the notch receptor thus causing the release of inflammatory mediators via macrophages. As notch can regulate macrophage-mediated inflammation it can serve as a therapeutic target for diabetic foot ulcers.

Conclusion: This review focuses on the effect of notch on various cell mediators and phases of diabetic wound healing and deals with how notch activation or inhibition can serve as a potential therapeutic target for healing diabetic foot ulcers.

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1. Introduction

Type 2 diabetes (formerly called non-insulin-dependent, or adult-onset) results from the body's inability to utilize insulin. During 2000–16, there was a 5% increase in premature mortality from diabetes. In 2019, an estimated 1.5 million deaths were caused due to diabetes globally, 374 million people are at increased risk of developing type 2 diabetes. The number of patients with diabetes globally has increased from 108 million in 1980 to 422 million in 2014 [1]. Combined with reduced blood flow and neuropathy (nerve damage) in the feet, there is a significant, inevitable predisposition of foot ulcers, infection, and eventual need for limb amputation (see Table 1, Figs. 1–3).

Diabetic foot ulcer (DFU) is a major factor affecting the quality of patient's life. About 85% of all amputations in diabetic population are due to foot ulceration that eventually deteriorate into severe gangrene and infection i.e., approximately 1 out of 4 patients who are suffering with diabetes have the risk of developing a foot ulcer. Currently, limited options are available to deal with DFUs, since the current alternatives are expensive, complicated procedures (such as grafts) and deal with only prevention of infection (pharmacotherapy). Delayed healing of foot ulcers involves various mechanisms, which include microvascular complications of reduced blood supply, reduced proliferation and migration of keratinocytes and fibroblasts, reduced production of endothelial progenitor cells and reduced angiogenesis [2]. Besides, the dysregulation of certain signaling pathways such as overproduction of cytokines which

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Original Article

Subtle Intricacies Identified during Streptozotocin-Induced Diabetes in Wistar Rats

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ABSTRACT

Aim: This study aimed to establish the dose of streptozotocin required to induce Type -1 diabetes in Wistar rats. **Background:** Streptozotocin is currently employed worldwide to induce insulin-dependent diabetes mellitus also known as Type 1 diabetes mellitus in experimental animals. Though many reports on the use of streptozotocin induction of diabetes are reported in the literature, they were not reproducible. Moreover, there was no mention of the mortality associated with the same as well as the conditions followed during the study. **Materials and Methods:** In the present study, the dose, route, and solvent used for streptozotocin were investigated. Various doses of streptozotocin 55, 50, 40, and 35mg/kg dissolved in either freshly prepared cold 10mM sodium citrate buffer (pH 4.5) or normal saline solution was administered intraperitoneally as well as intravenously. For intraperitoneal administration, the dose-volume was 10mL/kg whereas for intravenous administration the dose-volume was 2mL/Kg. Different routes were employed to ascertain the cause of mortality for which an autopsy was performed. Besides mortality rate was also determined. **Results and Discussion:** The findings of the study revealed that a 35-40mg/kg dose of streptozotocin showed less percentage mortality and successful induction of diabetes. **Conclusion:** Mortality (10-20%) was observed at a dose of 35-40mg/kg streptozotocin. Therefore, streptozotocin (35-40mg/kg) was confirmed to be safe and effective for the induction of diabetes in Wistar rats. This paper highlights subtle intricacies observed during induction of diabetes in Wistar rats using streptozotocin

Keywords: Male Wistar rats, Streptozotocin, Type-1 diabetes, 5% dextrose, Mortality, Normal saline solution.

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INTRODUCTION

Streptozotocin (STZ) is currently employed worldwide to induce insulin-dependent diabetes mellitus (IDDM), also known as Type 1 Diabetes Mellitus (T1DM) in experimental animals. However, despite meticulously following protocols for STZ induction of diabetes as published in the literature, a high percentage of mortality was observed in experimental animals. Alarmed with the high percentage of mortality, the authors decided to put across their findings which could help researchers attempting to induce diabetes in experimental animals as none of the papers mentioned the mortality rate after STZ administration. Also, certain conditions to be followed post-STZ administration was not documented. Based on the literature survey conducted, various doses of STZ have been employed (40,[1-3] 45,[4-8] 50,[9] 55,[10-13] 60,[14-18] 65[19-22] mg/kg), (Table 1) to induce diabetes in Wistar rats. STZ was mostly dissolved in 10 mM sodium citrate buffer (pH 4.5) and a few instances in normal saline solution.[23-28] Though 10mM sodium citrate buffer pH (4.5) was commonly employed as a solvent to dissolve STZ, the mortality percentage and cause of mortality associated with these methods were not documented. Therefore, researchers attempting STZ for diabetes induction face problems due to a lack of information regarding mortality and experimental conditions to be followed. This study was carried out to establish diabetes in Wistar rats following the STZ dose reported in the literature. In this study, we investigated mortality percentage and cause of mortality with the administration of STZ in various doses reported in the literature. Moreover, we also investigated suitable solvents for STZ. STZ was injected intravenously as well as intraperitoneally in Wistar rats to compare and ascertain the cause of mortality following STZ injection.

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