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Antineoplastic properties of zafirlukast against hepatocellular carcinoma via activation of mitochondrial mediated apoptosis

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Highlights

- Anti-HCC potential of zafirlukast.
- Zafirlukast triggers iNOS/eNOS mediated mitochondrial apoptosis pathway.
- Restoration of perturbated metabolites to normal using ^{1}H-NMR based metabolomics.

Abstract

Hepatocellular carcinoma (HCC) is one of the most common cancers worldwideand haslimited treatment options. In view of this, zafirlukast (ZAF) was administered orally to DEN-induced HCC rats to evaluate its antineoplastic properties. ELISA, qRT-PCR and Western blot were used to determine the molecular mechanism associated with ZAF therapy for HCC. We found that HCC developed as a result of lower expression of caspases 3 and 9, but their levels returned to normal when the expression of eNOS, BAX, BAD, and Cyt C was decreased and when the expression of

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Antioxidants & Redox Signaling, VOL. 0, NO. ja |

normal

Malabaricone C attenuates NSAID-induced gastric ulceration by reducing oxidative/nitrative stress and inflammation and promoting angiogenic auto-healing

Dr. Biswanath Maity, Ms. Madhuri Basak, Mr. Tarun Mahata, Ms. Sreemoyee Chakraborti, Mr. Pranesh Kumar, Dr. Bolay Bhattacharya, Prof. sandip kumar bandyopadhyay, Prof. Madhusudan Das, Dr. Adele Stewart, and Dr. Sudipta Saha

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Abstract

Aims: Non-steroidal anti-inflammatory drugs (NSAIDs), amongst the most commonly used drugs worldwide, are associated with gastrointestinal complications that severely limit the clinical utility of this essential class of pain medications. Here, we mechanistically dissect the protective impact of a natural product, malabaricone C, on NSAID-induced gastropathy. Results: Malabaricone C dose dependently diminished erosion of the stomach lining and inflammation in mice treated with NSAIDs with the protective impact translating to improvement in survival. By decreasing oxidative and nitrative stress, malabaricone C treatment prevented NSAID-induced mitochondrial dysfunction and cell death; NF-κB induction, release of pro-inflammatory cytokines and neutrophil infiltration; and disruptions in the vascular endothelial growth factor/endostatin balance that contributes to mucosal auto-healing. Importantly, malabaricone C failed to impact the therapeutic anti-inflammatory properties of multiple NSAIDs in a model of acute inflammation. In all assays tested, malabaricone C proved as or more efficacious than the current first line therapy for NSAID-dependent GI complications, the proton pump inhibitor omeprazole. Innovation and Conclusion: Given that omeprazole-mediated prophylaxis is, itself, associated with a shift in NSAID-driven GI complications from the upper GI to the lower GI system, there is a clear and present need for novel therapeutics aimed at ameliorating NSAID-induced gastropathy. Malabaricone C provided significant protection against NSAID-induced gastric ulcerations impacting multiple critical signaling cascades contributing to inflammation, cell loss, extracellular matrix degradation, and angiogenic auto-healing. Thus, malabaricone C represents a viable lead compound for the development of novel gastroprotective agents.

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Preparation and Evaluation of Tapentadol Hydrochloride Solid Lipid Nanoparticles

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ABSTRACT

Tapentadol Hydrochloride is a centrally acting opioid analgesic used for the treatment of musculoskeletal pain. The aim of the present study is to release the drug at a controlled rate by formulating solid lipid nanoparticles using Hot Homogenization method. In the present study SLN's are prepared by using Glycerol Monostearate and Stearic acid as lipids and Poloxamer-188 as stabilizer in different ratios in order to get the optimized formulation. The solid lipids and drug were evaluated for drug interactions by using FTIR, DSC, and surface morphology by SEM in order to select the effective formulation. The prepared formulations (F1-F12) were evaluated for Particle size, Zeta potential, %Entrapment efficiency, *in vitro* drug release studies and stability studies. The FTIR spectra revealed that there is no significant interaction between the drug and lipids. SEM images revealed that the particles are spherical in shape with smooth surface. The particle size was found as 101.9 nm, Zeta potential was found as -18.1mV, % Entrapment Efficiency (%EE) was found as 88.7±0.36 and the % drug release was found as 97.8±0.60 in 10 hours following first order release kinetics and Higuchi model. The Tapentadol Hcl loaded SLN's of F3 formulation shows more effective when compared to all the other formulations. All the results shows that the Tapentadol Hcl SLN's can be effectively used for treating severe pain by controlling the rate of release at the targeted site.

Keywords: Tapentadol Hydrochloride, Glycerol Monostearate, Stearic acid, Poloxamer-188, Hot Homogenoisation method.

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INTRODUCTION

Nanoparticles are the colloidal carriers ranges in the size of 10-1000 nm prepared by using natural/ synthetic polymers in order to target the drug at the specific site and to release the drug at controlled rate. To overcome the toxicity and the high cost of the polymer solid lipids has been put forward to prepare solid lipid nanoparticles [1].

Solid lipid nanoparticles (SLN's) were introduced in 1991 which represent an alternate carrier system to the traditional colloidal carriers such as emulsions, liposomes, polymeric microspheres and polymeric nanoparticles. Nanoparticles made from solid lipids are attracting major attention as novel colloidal drug carrier for intravenous applications as they have been proposed as an alternative particulate carrier system [2]. This system consists of spherical solid lipid particles which ranges in the size of nanometer, dispersed in aqueous surfactant solution. Generally, the solid lipids are made of hydrophobic core having a single layer of phospholipids coating. These solid lipid nanoparticles have potential of carrying both lipophilic drugs and hydrophilic drugs as they are amphipathic in nature [3].

Neuropathic pain (NP) has been defined as "pain caused by a lesion or disease of the somatosensory nervous system. NP is a common condition that results from various aetiologies and can be categorised into either peripheral or central NP syndromes. Central NP is the result of a central lesion or disease such as stroke, multiple sclerosis or spinal cord injury, whereas peripheral NP occurs from dysfunction or damage to peripheral nerves. [4]. Tapentadol Hydrochloride is a centrally acting opioid analgesic used for the treatment of neuropathic pain. It belongs to the class of benzenoids with dual mechanism of action as an agonist of the μ-opioid recptor and as a norepinephrine reuptake inhibitor. It's bioavailability is about 32% with an elimination half-life of about 4 hours [5]. In the present study solid lipid nanoparticles are prepared and loaded with tapentadol hydrochloride in order to release the drug at the targeted site at a controlled rate.

MATERIALS AND METHODS

Materials

Glycerol Monostearate and Stearic Acid was obtained from Qualikems fine chem. Pvt. Ltd., Vadodara, Gujarat, India and

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ANALYTICAL METHOD DEVELOPMENT FOR SIMULTANEOUS ESTIMATION OF RITONAVIR AND LOPINAVIR IN TABLET DOSAGE FORMS BY RP – HPLC

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ABSTRACT

A simple accurate and precise analytical method was developed for the simultaneous estimation of Ritonavir and Lopinavir in its tablet dosage form by RP-HPLC. This both combination drug has anti-retroviral agents and hence is used for the therapy of human immunodeficiency virus infection in adults and pediatric patients. Mobile phase with degassed methanol: potassium dihydrogen phosphate (KH2PO4) buffer 55:45V/V was run through standard discovery, Inertsil C18 column(4.6x150mm,5µm) column at a rate of 1ml/min at 25°C and optimized wavelength was 275nm.Retention time for Ritonavir and Lopinavir was 2.997min and 4.370min, %RSD of 0.2% and %recovery of 0.6% were obtained for Ritonavir and Lopinavir respectively. LOD and LOQ values obtained for Ritonavir and Lopinavir. All parameters of validation are found inside the range and method was precise and reliable which is also economical that can be adopted in regular quality control test in Industries.

KEYWORDS: Lopinavir, Ritonavir, RP-HPLC.

INTRODUCTION

The combination of lopinavir and ritonavir is used with other medications to treat human immunodeficiency virus (HIV) infection. Lopinavir and ritonavir are in a class of medications called protease inhibitors. They work by decreasing the amount of HIV in the

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METHOD DEVELOPMENT AND VALIDATION FOR AMLODIPINE BESYLATE AND CARVEDILOL IN COMBINE PHARMACEUTICAL DOSAGE FORMS BY RP-HPLC

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ABSTRACT

A new method was established for simultaneous estimation of a Amlodipine Besylate and Carvedilol by RP-HPLC method. The chromatographic conditions were successfully developed for the separation of Amlodipine Besylate and Carvedilol by using Inertsil - ODS C18(250 x 4.6 mm, 5µ), flow is 1.0 ml/min, mobile phase ratio was Phosphate buffer and Methanol (30:70), detection wave length was 254 nm. Chromatogram observed at RT's of 3.661min to Amlodipine Besylate and 6.453min to Carvedilol.

KEYWORDS: Amlodipine Besylate and Carvedilol, RP-HPLC, Acetonitrile

INTRODUCTION

In liquid chromatography, the solute retention is governed by the solute distribution factor, which reflects the different interactions of the solute – stationary phase, solute – mobile phase and the mobile phase – stationary phase .For a given stationary phase, the retention of the given solute depends directly upon the mobile phase, the nature and the composition of which has to be judiciously selected in order to get appropriate and required solute retention. The mobile has to be adapted in terms of elution strength (solute retention) and solvent selectivity (solute separation) Solvent polarity is the key word in chromatographic separations since a polar mobile phase will give rise to low solute retention in normal phase and high solute retention in reverse phase LC. For the greatest sensitivity λ_{max} should be used. Higher wavelengths give greater selectivity.

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A STUDY OF PRICE VARIATION AMONG THE VARIOUS BRANDS OF DRUGS UNDER DIFFERENT CATEGORIES OF CVS AND CNS AVAILABLE IN INDIAN PHARMACEUTICAL MARKET

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ABSTRACT

The price of the drug plays a key role in India. This study was aimed to analyse the cost ratio and percentage price variation among various brands of drugs under central nervous system and cardiovascular drugs available in the Indian market. Cost of central nervous system and cardiovascular drugs manufactured by different pharmaceutical companies, in the same strength and dosage forms was obtained from "current index of medical specialties" April-July 2018" issue and "Indian Drug Review" Volume. XXIV, Issue No.5, 2018 to analyze the maximum and minimum price analysis INR 10 tablets was calculated. The study shows that there is a wide variation in the prices of different brands of cardiovascular system the highest cost ratio (1:2.79) and percentage price variation (179.27) was found for clopidogrel 75mg and central nervous system the highest cost ratio (7.66) and percentage price variation (161.09) was found for Alprazolam 0.25 mg. There is a wide difference in the cost of different brands of central nervous system and cardiovascular drugs available in India. The clinicians prescribing these drugs should be aware of these variations in cost to reduce the cost of drug therapy. This in turn reduces the economic burden on the patients.

KEYWORDS: price variation, cost ratio, central nervous system, cardiovascular drugs.

INTRODUCTION

The pharmaceutical industry has grown rapidly in India for decades. Indian market floods with a large number of branded medicines from local and foreign manufacturers.[1,2]

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NEW RP-HPLC METHOD DEVELOPMENT AND VALIDATION FOR SIMULTANIOUS ESTIMATION OF VILDAGLIPTIN AND METFORMIN HCL IN PHARMACEUTICAL DOSAGE FORM

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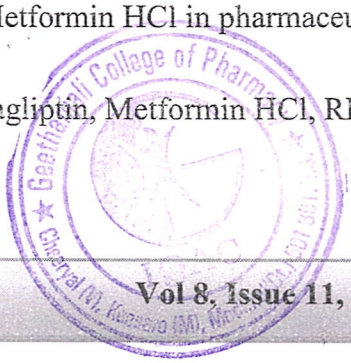
ABSTRACT

Objective: A New method was established for simultaneous estimation of Vildagliptin and Metformin HCl by RP-HPLC method. **Methods**: Chromatographic separations were carried using column AGLIENT HPLC (1100) with the E-Z Chrome Software with PDA detector with a mobile phase composition of 0.1 M Na_2HPO_4 and Acetonitrile have been delivered at a flow rate of 1ml/min and the detection was carried out using waters HPLC auto sampler, separation module 2695 HPLC system with PDA detector at wavelength 210nm. **Results**: The retention time for Vildagliptin and Metformin HCl were 6.639 and 2.653 minute respectively. The correlation coefficient values in linearity were found to be 0.999 and concentration range 50-200µg/ml for Vildagliptin and 50-200µg/ml for Metformin HCl respectively. For accuracy The total recovery was found to be 99.5 % and 99.7% for Vildagliptin and Metformin HCl. LOD and LOQ for Vildagliptin 0.0052µg/mL and 0.0158µg/ml. LOD and LOQ for Metformin HCl 0.219µg/mL and 0.665µg/ml. **Conclusion**: The results of study showed that the proposed RP-HPLC method is a simple, accurate, precise, rugged, robust, fast and reproducible, which may be useful for the routine estimation of Vildagliptin and Metformin HCl in pharmaceutical dosage form.

KEYWORDS: Vildagliptin, Metformin HCl, RP-HPLC, Simultaneous estimation.



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METHOD DEVELOPMENT AND VALIDATION FOR TAZOBACTAM AND PIPERACILLIN IN COMBINE PHARMACEUTICAL DOSAGE FORMS BY RP-HPLC

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ABSTARCT

A new method was established for simultaneous estimation of a Tazobactamand Piperacillin by RP-HPLC method. The chromatographic conditions were successfully developed for the separation of Tazobactamand Piperacillin by using Inertsil -ODS C18 (250 x 4.6 mm, 5µ), flow is 1.0 ml/min, mobile phase ratio was Methanol: Buffer (80:20), detection wave length was 225 nm.

KEYWORDS: Tazobactam and Piperacillin, RP-HPLC, Acetonitrile.

INTRODUCTION

In liquid chromatography, the solute retention is governed by the solute distribution factor, which reflects the different interactions of the solute – stationary phase, solute – mobile phase and the mobile phase – stationary phase. For a given stationary phase, the retention of the given solute depends directly upon the mobile phase, the nature and the composition of which has to be judiciously selected in order to get appropriate and required solute retention. The mobile has to be adapted in terms of elution strength (solute retention) and solvent selectivity (solute separation) Solvent polarity is the key word in chromatographic separations since a polar mobile phase will give rise to low solute retention in normal phase and high solute retention in reverse phase LC.

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NEW RP-HPLC METHOD DEVELOPMENT AND VALIDATION FOR SIMULTANIOUS ESTIMATION OF VILDAGLIPTIN AND METFORMIN HCL IN PHARMACEUTICAL DOSAGE FORM

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KEYWORDS: Vildagliptin, Metformin HCl, RP-HPLC, Simultaneous estimation.

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Synthesis and antimicrobial activity of salicylaldehyde Schiff bases from aromatic amines

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ABSTRACT

A new efficient and environmentally friendly procedure for the synthesis of a series of salicylaldehyde-based Schiff bases under conventional method is described. The method is compared with the microwave irradiation method also. The present work involves condensation of salicylaldehyde with various aromatic amines in water under the conventional method. A judicious choice of the solvent and reaction conditions allowed the final products to be generated in excellent yields in a one-step procedure, whereas experiments under thermal conditions led to lower yields with tedious work-up. The conventional method gives advantages like reduction in reaction time, increase in conversion, reduced wastes, and good yields.

Keywords— *B. subtilis, DMSO*

1. INTRODUCTION

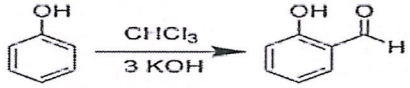
A Schiff base (named after Hugo Schiff) is a compound with the general structure R2C=NR'. They can be considered a sub-class of imines, being either secondary keto imines or secondary aldimines depending on their structure. The term is often synonymous with azomethine which refers specifically to secondary aldimines. Schiff bases derived from aromatic amines and aromatic aldehydes have a wide variety of applications in many fields, biological, inorganic and analytical chemistry. Applications of many new analytical devices require the presence of organic reagents as essential compounds of the measuring system. Schiff bases are aldehyde- or ketone-like compounds in which the carbonyl group is replaced by an imine or azomethine group. They are widely used for industrial purposes and also exhibit a broad range of biological activities. This short review compiles examples of the most promising antimalarial, antibacterial, antifungal, and antiviral Schiff bases. An overview of synthetic methodologies used for the preparation of Schiff bases is also described.

2. SALICYLALDEHYDE

Salicylic aldehyde (2-hydroxybenzaldehyde) is the organic compound with the formula C_6H_4CHO-2-OH. Along with 3-hydroxybenzaldehyde and 4-hydroxybenzaldehyde, it is one of the three isomers of hydroxybenzaldehyde. This colourless oily liquid has a bitter almond odour at higher concentration. Salicylaldehyde is a keyprecursor to a variety of chelating agents, some of which are commercially important.

2.1 Production

Salicylaldehyde is prepared from phenol and chloroform by heating with sodium hydroxide or potassium hydroxide in a Reimer–Tiemann reaction:



Alternatively, it is produced by condensation of phenol or its derivatives with formaldehyde to give hydroxybenzyl alcohol, which is oxidized to the aldehyde.

2.2 Natural occurrence

Salicylaldehyde was identified as a characteristic aroma component of buckwheat. It is also one of the components of castoreum, the exudate from the castor sacs of the mature North American beaver (Castor canadensis) and the European beaver (Castor fibre), used in perfumery. Furthermore, salicylaldehyde occurs in the larval defensive secretions of several leaf beetle species that belong

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FORCED DEGRADATION STUDIES OF IRBESARTAN AND ANALYSIS OF ITS FRAGMENTS

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ABSTRACT

Forced degradation studies include the degradation of drug substances and drug product at conditions more severe than the accelerated conditions. The purpose of this study is to know the exact shelf life of the anti-hypertensive drug irbesartan under various conditions like ambient condition, humidity, temperature, photo light and analysis of its parameters as per ICH guidelines. The forced degradation studies were carried out on hydrolysing the drug substance within the sight of water, acid and base shows no significant change in the peak purity indicating that the API is stable and does not undergo any changes due to hydrolysis. The same observation was achieved in case of forced degradation by oxidation. The peak purity matches with the mother sample but on hydrolysis, acid and oxidation degradation IMPURITY-3 has been identified and on base degradation IMPURITY-A has been identified. The project will be further studied what kind of Impurity and how it was developed.

KEYWORDS: Irbesartan, Degradation Studies, ICH guidelines.

INTRODUCTION

An impurity as defined by the ICH (The International Conference on Harmonisation Technical Requirements for Registration of Pharmaceuticals for Human Use) guidelines is "any component of medical product which is not the chemical entity defined as the active substance or excipient in the product.[1]

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HEB JOHP

A PROSPECTIVE CROSS-SECTIONAL STUDY ON PRESCRIBING PATTERN OF ANTIBIOTICS AND ANALGESIC DRUGS IN ORTHOPEDICS DEPARTMENT AT TERTIARY CARE HOSPITAL

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ABSTRACT:

The present study was taken up to generate useful data by analyzing pooled information regarding the prescribing pattern of NSAID's and antibiotics such as formulations, dose, route, frequency, duration of administration, Concomitant medication, FDC and average number of drugs per prescription and also assessed to check whether the drugs prescribed were enlisted under NLEM, India 2015 or not. To calculate the number of drugs per prescription by the generic name and brand name. To determine the average number of drugs per prescription of analgesics and antibiotics. To determine the category of analgesic and antibiotics drugs having a better therapeutic effect in orthopedics cases. The study was designed as a prospective, observational; evaluating the prescribing pattern concerned with the use of analgesics and antibiotics in orthopedics department.The study was conducted in a single centred 300 bedded hospital in Orthopaedics department. 102 prescriptions were collected and analyzed prospectively for the pattern of NSAID and antibiotics for arthritic and non-arthritic conditions; the drug formulation, route, Dosage frequency, duration of admission and concomitant medications. Duration of treatment, percentage of drugs prescribed from essential drugs list or formulary, the drugs were included in NLEM 2015 was found to be rational, there was no misuse of antibiotics and there was no polypharmacy noticed. Of 102 prescriptions 51 cases were from OPD and 51 cases were from IPD. The study was undertaken to give feedback to the prescribers, so as to create awareness about the over-use of drugs especially antibiotics hence patient counselling should be done for proper use of antibiotics, culture sensitivity tests should be conducted before prescribing antibiotics. NSAIDs were prescribed empirically for various arthritic and Non-arthritic conditions, frequently with various adjuvants' as per the standard guide lines. NSAID's are having better therapeutic effect in substituting the pain compared to Opioids.

Key words: Analgesics, Antibiotics, WHO list of essential medicines, National Model List of Essential Medicines (NLEM), Orthopedics, Prescription Pattern, NSAIDs (Non steroidal anti-inflammatory drugs).

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CURRENT TRENDS IN PHARMACEUTICAL COUNTERFEITS WITH ADVANCED TRACE AND TRACK TECHNOLOGY

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ABSTRACT

Pharmaceutical counterfeiting is becoming a serious problem both in developed and in developing countries. This paper considers the extent of the problem and provides several examples of drugs, which have been counterfeited. Additionally, the effects of counterfeit products on consumers, health care providers, drug manufacturers and governments are discussed. Several of the currently used methods for the detection of anti-counterfeiting technologies is out lined. Finally, pharmaceutical anti-counterfeiting measures such as the use of holograms, tracers and taggant, electronic tracking and Rfid technologies have summarized.

DEFINATION

- The World Health Organization (WHO) has defined that counterfeit medicines is the fake medicine. It may be contaminated or may contain wrong or no active ingredient. They could have the right active ingredient but the wrong dose. Counterfeit drugs are illegal and may be harmful to health.
- According to US law, counterfeited medicine is pharmaceutical product, which is produced and sold with the intent to deceptively represent its origin, authentically or effectiveness.

INTRODUCTION

The matter of fake medications is certainly not another one to the world in spite of the fact that it proceeding all through the ages. The issue of fake medications distinguished during the 1980s and as of late the issue has heightened numerous more cases are happening in the

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REGULATORY GUIDELINES FOR APPROVAL OF BIOSIMILARS IN INDIA, UNITED STATES AND EUROPE - A COMPREHENSIVE SUMMARY

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ABSTRACT

A biosimilar is a biological medicine similar, but not identical, to an already registered reference bio therapeutic product in terms of quality, safety, and efficacy. These drugs are also called as biosimilar products, follow-on protein products and subsequent-entry biologics. EMA (European Medicines Agency) was the first to introduce the guidelines for biosimilar approval, effective from June 2006. Biosimilar guideline was released in 2012 in India. The United States enacted the Biologics Price Competition and Innovation Act (BPCI) in the end of March 2010 to providing an application pathway for follow-on biological products under sections 7001 to 7003 of the Patient Protection and Affordable Care Act and also codified in 42 USC 262(k). In Europe, in 2001, legislation concerning biosimilar was codified as Directive 2001/83/EC to create a new marketing authorization procedure for similar biological medicinal products and also Committee for Medicinal Products for Human Use (CHMP) of the EMA is concern with these biosimilar products. In India, Review Committee on Genetic Manipulation (RCGM) and Genetic Engineering Approval Committee (GEAC) of Central Drugs Standard Control Organization (CDSCO) is responsible for the development and preclinical evaluation of recombinant biologics drugs. This article having precise, concise, and simple comparison of US, Europe and India related to biosimilar drugs regulations and litigation.

KEYWORDS: Biosimilars, CDSCO, USFDA, EMA, Regulations, Litigation.

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FABRICATION AND ASSESSMENT OF LEVOFLOXACIN CONTROLLED RELEASE MATRIX TABLETS

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Abstract:

Vividly Oral drug delivery method is the most widely utilized routes for administration among all alternatives that have been explored for systemic delivery of drug via various pharmaceutical products of different dosage forms. Popularity of the route may be ease of administration as well as traditional belief that by oral administration the drug is due to the well absorbed into the food stuff ingested daily. The present work is aimed at preparing and evaluating Controlled-release (CR) matrix tablets of Levofloxacin using different polymers. From the results, formulationf6 containing Levofloxacin 250 mg. Xanthum gum evolved as the optimized formulation. The result revealing shows the feasibility of fabricating levofloxacin controlled release tablets significantly with better drug release profile.

Keywords: *Controlled release tablets, Levofloxacin, Fabrication & drug release.*

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COMPLICATED PRESENTATION OF PIERRE ROBIN SYNDROME- A CASE REPORT

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PRESENTATION OF CASE

A 15-year-old girl student presently a 10th grader from a state high school was diagnosed with Pierre Robin syndrome during the first month of life, thus was informed that she had not been immunised since birth. A detailed history was obtained, which revealed that she had complaints of flattering weight, severe malnutrition and respiratory distress and no history of neuro-developmental delay. Family history: twins were born, the other twin passed away (stillbirth), and no apparent congenital anomalies found.

Thus, past data was found to be that she had a history of halitosis and hearing abnormalities. On subject interrogation, there was no history of recurrent cold or cough, spinal abnormalities, bowel, and bladder dysfunction.

The child was dysmorphic; had lower centiles of her BMI for her age, pallor of skin, retrognathia, crowned teeth, and mandible deformity. Cardiovascular system examination- no murmur. No abnormality was detected on two-dimensional echocardiography. Hence, mandibular osteotomy was done carefully after correction of anaemia by considering all the above conditions. The child improved and got discharged within a week.

CLINICAL DIAGNOSIS

Pierre Robin Syndrome.

DIFFERENTIAL DIAGNOSIS

- Stickler syndrome.
- Velocardiofacial syndrome.
- Treacher Collins syndrome.

PATHOLOGICAL DISCUSSION

Pierre Robin sequence (PRS) presents with the association of micrognathia, glossoptosis, and airway obstruction, this condition occurs at birth, and cannot be acquired in later developmental stages. In 1934 a French physician reported the association with cleft palate and this constellation of findings later termed it as a syndrome.[1]

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Epidemiological studies reveal that Pierre Robin syndrome is a rare and complex syndrome which has been affecting one in 8,500 to 14,000 births also there is a higher incidence for twins and hence, no gender differences identified. Multiple congenital disabilities have commonly been described, which correlates with inadequate growth of the lower jaw. Also, to help in recovering up weight loss and feeding difficulties, a nasogastric tube for feeding is essential to gain weight.[2]

The Complete Blood Picture of the child revealed Hb- 10.3 gms %, which confirms anaemia and Ionised Calcium- 1.11 mmol/L, which significantly shows a lower level of calcium. Also, the child developed the complication of TMJ Ankylosis right side, which is further corrected by osteotomy operative procedure. Since a long time ago, she had feeding difficulties, which is very common in patients presenting with PRS. Hence this reflected with her compromised immunity; thereby, it can be corrected by a surgical procedure. Mandibular Osteotomy procedure executed, which shows mandible correction is done to widen the Jaw space. (Fig. 1) The lateral view displays the rods positioned post-surgery. (Fig. 2)

PRS patients will be barred from the mandibular distraction when they present with other anomalies such as central apnoea, neurologic compromise, multilevel airway obstruction, or airway oedema from severe reflux. In patients who are not qualified for mandibular distraction, a tracheostomy is done in the neonatal period. Some patients may later resolve their abnormalities and then be offered a mandibular distraction to facilitate decannulation.[3]

Two PRS cases that developed severe upper airway obstruction immediately after birth and were rescued by fiberoptic nasotracheal intubation.[4] Numerous theories have been explained this syndrome among them; the mechanical theory is most popular. This theory considers the impact of various external factors on the fetus in the intrauterine period. Furthermore, the mechanical theory gets accomplished by the neurological theory and the genetic theory. Hence the neurological theory refers to delay in nerve maturation which is observed in the electromyography from the tip of the tongue. Finally, the genetic theory suggests the fact that this syndrome might be associated with chromosomal deletions. Among the various medical problems encountered the utmost important ones in this syndrome remain breathing difficulties, (Dyspnoea) and eating disorders.[5]

Pierre Robin sequence (PRS) is a congenital abnormality which is characterised by the presence of a combination of

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DIFFICULTIES AND CHALLENGES IN BUSINESS WRITING OF THE MANAGEMENT STUDENTS

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ABSTRACT

The face of business communication has transformed drastically for the last few years. The present paper attempts to trace out the problems and challenges of written business communication to the management students who are from different professional colleges in Telangana region of India. The students, who are enrolled in master's program and studying second year. The paper explores the students' attitude towards writing and their priorities in learning business writing. The data were collected by administering the questionnaires to the management students from various professional management colleges for the investigation of learners' views, opinions and experiences about business writing. In order to find out their problems and difficulties faced during business writing, a descriptive test was also conducted for 10 management students. Later, the data was analyzed using the quantitative method approach. With the analysis of data, it was found that writing skills of students were totally neglected throughout their academics and it was also discovered that writing was used for various purposes such as to complete assignments, writing exams and to take part in other classroom writing activities. It is observed that the students' writing skills were found to be poor in business communication especially in business writing. It was also found that most of the classroom instruction was teacher-centric where the students' role was limited and they were passive most of the time in the classroom. Usually, the writing activities were conducted individually, ignoring the pair and the group activities. However, the learners treated writing as an activity for accomplishing assigned tasks and submit them in time for the teacher's evaluation. In the end, the study is also suggested that teachers should create teaching writing context/activities more interestingly. So, that all the learners do take part in all the classroom activities/tasks enthusiastically, enhance their business writing skills and produce effective writing skills in their day to day lives.

KEYWORDS: *Writing Skills, Business Writing, Business Written Communication, Writing Problems*

INTRODUCTION

New technologies have been flooding constantly, evolving and developing in the areas of language teaching that means the change in the way of communication. With the evaluation of technology, the face of business communication has transformed drastically for the last decade. The students use advanced gadgets for writing before they enter into the college/workplace. Communication is the key to success in any business context. Good business writing adds to the credibility of the students and reflects in their writing. It is perceived that people who cannot communicate well in writing are not considered for employment, promotion or higher positions. The most common forms of communication in business are spoken and written, these regarded as productive language skills.

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Case Report

ALENDRONATE-INDUCED RESPIRATORY DISTRESS

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ABSTRACT

Respiratory distress is a rare adverse effect of alendronate that is typically associated with severe dyspnoea and wheezing and typically requires hospitalization. The patient with a history of dyspnoea and wheezing during the strenuous workload was treated promptly with alendronate for newly diagnosed osteoporosis. After 2 days, respiratory distress complications were restarted and we accurately reported the patient with basophilia, elevated immunoglobulin E (with a blood test), and allergic bronchopulmonary aspergillosis (with computed tomography scan image). The prospective patient was adequately understood as alendronate-induced respiratory distress with an unfortunate rechallenge method. Although there is no direct causal relationship from this adverse case report, the possible mechanism has discussed typically based on peer-reviewed literature.

Keywords: Alendronate, Respiratory distress, Dyspnoea, Wheezing, Allergic bronchopulmonary aspergillosis, Basophilia, Elevated immunoglobulin E.

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INTRODUCTION

Alendronate is a specific osteoclast inhibitor used in the preferential treatment of osteoporosis and has a place with the class of bisphosphonates. It works by forestalling the resorption of bone. Alendronate is not indicated for use in pediatric populations [1]. Alendronic acid binds to bone hydroxyapatite in which endocytic vesicles are fermented, promptly releasing alendronic acid to the cytosol of osteoclasts, where they instigate apoptosis [2]. Adverse impacts of alendronate, for example, dyspepsia to esophageal stricture, muscle torment, influenza-like disorder, and vertigo, have been accurately accounted [3]. Liquor, cocaine, amphetamines, sedatives, and benzodiazepines are the most normally manhandled drugs that may instigate intense respiratory distress [4], yet alendronate is the medication which is recently revealed as causing respiratory distress, for example, dyspnea and wheezing.

CASE REPORT

A 50 year-elderly male person was conceded in casualty with dyspnea and wheezing. He works laboriously in the coal mine shafts and had a social history of smoking for 5 years. His clinical history was seen with troubled breath during strenuous physical action from the most recent 2 years and had been well controlled with inhaled salbutamol. He is not an asthmatic patient prior, however, feels labored breath during physical pressure. He likewise diminished his strenuous workload in coal mine shafts and denied having troubled breath from the past 1 year and quitted salbutamol inhalation. The patient was diagnosed as osteoporosis just 10 days to his prior admission and started alendronate 10 mg po every day. Following 2 days, the patient was admitted in casualty with wheezing and dyspnea. His vital signs were respiratory rate – 31 breaths/min, oxygen saturation – 94%, pulse – 110 beats/min, circulatory strain – 130/70 mm Hg, and temperature – 37°C. His breath sounds were diminished and expiratory phase prolonged. The cardiovascular assessment was noteworthy for tachycardia. His physical examination was normal. The patient's chest radiography and electrocardiogram were normal. Consequences of his renal and liver capacity tests and urinalysis were also normal. Blood picture demonstrated normal range of hemoglobin – 14.0 g/dL, hematocrit – 45%, white blood cell count – 8000 cells/m^3, and platelets – 300,000/m^3. He was reported with elevated levels of basophils – 0.69 (reference range 0.04–0.4) and serum immunoglobulin E – 250 ng/mL (reference go 0–81 ng/mL). An infectious check C-reactive protein level, erythrocyte sedimentation rate, and microbiological exam of sputum were negative. The computed tomography (CT) scan picture reveals allergic bronchopulmonary aspergillosis and typically indicated focal varicoid bronchiectasis (Fig. 1). A factual finding of intense respiratory distress was made and supplemented with adequate oxygen. He was instantly treated with nebulized albuterol and intravenous hydrocortisone.

The likely patient improved within 24 h of admission and was discharged. With the suspicion of conceivable alendronate-induced respiratory complications, alendronate was stopped and the patient's past prescription was started. After the suspension of alendronate, he had no complaints for the following 3 weeks. As the patient was restarted with the symptoms of osteoporosis, he again administered the alendronate with recommendations from another doctor (who is unaware of his respiratory distress because of alendronate). After the second dose of alendronate, he again experienced dyspnea and wheezing within few hours and was admitted to the emergency department. Based on his readministered alendronate information and respiratory symptoms, he was restarted with albuterol and hydrocortisone. Within the very early hours of effective treatment, hypoxemia resolved.

DISCUSSION

This is a bizarre and uncommon case report of alendronate-induced respiratory distress. As per the Naranjo probability scale, alendronate was a reasonable justification for the patient's respiratory trouble right now [4]. Although no direct causal relationship can be drawn from this report, the relationship between the alendronate use and the beginning of the respiratory distress was promptly accepted because of alendronate, particularly with given consequences of an unfortunate rechallenge.

In the literature, there are a few published reports about alendronate that typically show a dose-dependent rise of histidine decarboxylase movement in different tissues (e.g., liver, lung, and spleen), prompting an expansion in histamine [5-7]. One of the other studies exhibits that basophils of selected patients with hypersensitive bronchopulmonary aspergillosis have marked cell hyperreactivity and patients with allergic bronchopulmonary aspergillosis had significantly more prominent histamine release to *Aspergillus* antigens [8]. This conversation result proposes a potential mechanism for worsening of an inflammatory reaction like respiratory distress because of histamine release [6] with

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Case Report

ALENDRONATE-INDUCED RESPIRATORY DISTRESS

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ABSTRACT

Respiratory distress is a rare adverse effect of alendronate that is typically associated with severe dyspnoea and wheezing and typically requires hospitalization. The patient with a history of dyspnoea and wheezing during the strenuous workload was treated promptly with alendronate for newly diagnosed osteoporosis. After 2 days, respiratory distress complications were restarted and we accurately reported the patient with basophilia, elevated immunoglobulin E (with a blood test), and allergic bronchopulmonary aspergillosis (with computed tomography scan image). The prospective patient was adequately understood as alendronate-induced respiratory distress with an unfortunate rechallenge method. Although there is no direct causal relationship from this adverse case report, the possible mechanism has discussed typically based on peer-reviewed literature.

Keywords: Alendronate, Respiratory distress, Dyspnoea, Wheezing, Allergic bronchopulmonary aspergillosis, Basophilia, Elevated immunoglobulin E.

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INTRODUCTION

Alendronate is a specific osteoclast inhibitor used in the preferential treatment of osteoporosis and has a place with the class of bisphosphonates. It works by forestalling the resorption of bone. Alendronate is not indicated for use in pediatric populations [1]. Alendronic acid binds to bone hydroxyapatite in which endocytic vesicles are fermented, promptly releasing alendronic acid to the cytosol of osteoclasts, where they instigate apoptosis [2]. Adverse impacts of alendronate, for example, dyspepsia to esophageal stricture, muscle torment, influenza-like disorder, and vertigo, have been accurately accounted [3]. Liquor, cocaine, amphetamines, sedatives, and benzodiazepines are the most normally manhandled drugs that may instigate intense respiratory distress [4], yet alendronate is the medication which is recently revealed as causing respiratory distress, for example, dyspnea and wheezing.

CASE REPORT

A 50 year-elderly male person was conceded in casualty with dyspnea and wheezing. He works laboriously in the coal mine shafts and had a social history of smoking for 5 years. His clinical history was seen with troubled breath during strenuous physical action from the most recent 2 years and had been well controlled with inhaled salbutamol. He is not an asthmatic patient prior, however, feels labored breath during physical pressure. He likewise diminished his strenuous workload in coal mine shafts and denied having troubled breath from the past 1 year and quitted salbutamol inhalation. The patient was diagnosed as osteoporosis just 10 days to his prior admission and started alendronate 10 mg po every day. Following 2 days, the patient was admitted in casualty with wheezing and dyspnea. His vital signs were respiratory rate – 31 breaths/min, oxygen saturation – 94%, pulse – 110 beats/min, circulatory strain – 130/70 mm Hg, and temperature – 37°C. His breath sounds were diminished and expiratory phase prolonged. The cardiovascular assessment was noteworthy for tachycardia. His physical examination was normal. The patient's chest radiography and electrocardiogram were normal. Consequences of his renal and liver capacity tests and urinalysis were also normal. Blood picture demonstrated normal range of hemoglobin – 14.0 g/dL, hematocrit – 45%, white blood cell count – 8000 cells/m^3, and platelets – 300,000/m^3. He was reported with elevated levels of basophils – 0.69 (reference range 0.01–0.1) and serum immunoglobulin E – 250 ng/mL (reference go 0–81 ng/mL). An infectious check C-reactive protein level, erythrocyte sedimentation rate, and microbiological exam of sputum were negative. The computed tomography (CT) scan picture reveals allergic bronchopulmonary aspergillosis and typically indicated focal varicoid bronchiectasis (Fig. 1). A factual finding of intense respiratory distress was made and supplemented with adequate oxygen. He was instantly treated with nebulized albuterol and intravenous hydrocortisone.

The likely patient improved within 24 h of admission and was discharged. With the suspicion of conceivable alendronate-induced respiratory complications, alendronate was stopped and the patient's past prescription was started. After the suspension of alendronate, he had no complaints for the following 3 weeks. As the patient was restarted with the symptoms of osteoporosis, he again administered the alendronate with recommendations from another doctor (who is unaware of his respiratory distress because of alendronate). After the second dose of alendronate, he again experienced dyspnea and wheezing within few hours and was admitted to the emergency department. Based on his readministered alendronate information and respiratory symptoms, he was restarted with albuterol and hydrocortisone. Within the very early hours of effective treatment, hypoxemia resolved.

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