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Development of Formulation and Rheological Studies for Palatable Dry Powder Suspension of Cefetamet Pivoxil Hydrochloride: A comprehensive review

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Abstract

The development of a palatable dry powder suspension of Cefetamet Pivoxil Hydrochloride is a safe and effective treatment for upper and lower respiratory tract infections in infants and children. This formulation helps to mask the unpleasant taste and sensitivity to moisture of Cefetamet Pivoxil Hydrochloride(CPH). Creaming index, Sedimentation volume, and flow rate of the reconstituted dry powder suspension were carried out as per the official methods. Various studies were conducted to understand the viscosity and flow behavior of the formulations, and microspheres of Cefetamet Pivoxil Hydrochloride, created using Eudragit E 100, were analyzed. The consistency indices and the flow behaviour index values of the formulations were found to be in the range of 21.72-74.19 and 0.36-0.45 respectively. The study concluded that a palatable Cefetamet Pivoxil Hydrochloride dry powder suspension formulation was successfully developed using sweetening, flavoring, and thickening agents. The optimized formulation, batch F2, complied with the Indian pharmacopoeia limits and exhibited an optimum viscosity for uniform mixing without lumps. Recommended storage between 2-8°C is advised, and the product remains stable at room temperature with a slight increase in viscosity.

Keywords: Cefetamet Pivoxil Hydrochloride, dry powder suspension, upper and lower respiratory tract infections, infants, Eudragit E 100 microspheres, scanning electron microscopy.

Introduction

A palatable Cefetamet Pivoxil Hydrochloride dry powder suspension (DPS) was formulated using various pharmaceutical ingredients including microcrystalline cellulose, sodium carboxy methyl cellulose and sodium saccharin. The spray dried Cefetamet Pivoxil Hydrochloride microspheres were characterized for various microscopic parameters. The effect of buccal mucosal penetration enhancer's mannitol, chitosan and sodium lauryl sulphate on the rheological properties of DPS was studied[1]. The maximum particle size was found to be 20.95±0.57µm with

sphericity index 0.75±0.048. The minor drug loss was observed in FT-IR (Fourier transform infrared spectroscopy) peaks signifies there is no interaction between drug and excipients. The Drug Excavation was performed using various solvents with continuous shaking. The maximum drug excavation was observed with methanol (93.87%) and acetone (91.54%). The mean pH of the product was found to be 6.92±0.12. The In-vitro Drug Diffusion Study of Drug and co-formulated products was done using the cellulose acetate membrane (0.45µm) in 0.1N-HCl medium. It was observed that there is a controlled release of drug from the synthesized microspheres compared to the free drug [2].

Rheological studies on 13 formulations containing chitosan sodium lauryl sulphate and buccal enhancer were performed using Brookfield viscometer and found to exhibit pseudo plastic flow with hysteresis loop and recovery memory. The addition of sodium lauryl sulphate and chitosan 3% w/v offers satisfactory consistent nature of the suspected formulations. Formulation prepared with sodium lauryl sulphate 1% and chitosan 3% w/v with better flow property for dry powder suspension sol with good palatability characteristics was developed from the study.

About 60% of children under six years of age have difficulty swallowing solid oral dosage forms. There is a critical need for drug formulations that can be swallowed unchewed. The formulation development and rheological studies of palatable Cefetamet Pivoxil Hydrochloride dry powder suspension are presented. Cefetamet Pivoxil Hydrochloride is a safe and effective drug for upper and lower respiratory tract infections in infants and children, but there is no suitable dosage form for toddlers who cannot swallow solid oral dosage forms[1]. Thus, a palatable dry powder suspension containing Cefetamet Pivoxil Hydrochloride was developed. Formulation floor was optimized by evaluating the sensory attributes and masking strategies of potential sweeteners. Then, batch DP-N1, the suspension with the active ingredient, excipients, and flavoring agent, was manufactured by direct blending. The trial suspension's consistency, particle size distribution, flowability, and rheological behavior were investigated [3].

Development of a palatable dry powder suspension of Cefetamet Pivoxil Hydrochloride – a semi-synthetic broad spectrum oral cephalosporin antibiotic of the third generation used to treat bacterial infections in children. Dry powder suspensions are preferred for Cefetamet Pivoxil Hydrochloride because this dosage form overcomes the bitterness and disinfectant taste of the drug palatably. The Ames test proved that the flavors and sweetening agents used in formulation development are non-mutagenic, comparing with the control. 4 Rheological studies of the formulations were carried out to know the viscosity and pseudoplastic behavior of the formulations. Eudragit RL 100 microspheres of Cefetamet Pivoxil Hydrochloride prepared by the emulsification solvent evaporation method were analyzed by scanning electron microscopy, percentage entrapment efficiency, in vitro diffusion and drug release kinetics studies revealed that the best formulation with 1:4 cold polymer-drug weight ratio was best suited for colon-targeting for the treatment of UC.

Cefetamet Pivoxil Hydrochloride: Properties and Applications

Cefetamet Pivoxil Hydrochloride is a third-generation cephalosporin, a β-lactam antibiotic with a broad range of antimicrobial activity against various pathogens

including Gram-positive and Gram-negative bacteria [2]. It is chemically described as (6R, 7R)−7-[[(2Z)-[[(4-carboxy-2-oxazolidin-3-yl)(4-hydroxy-phenyl)-(1-methylethyl)]methylene] amino] (2-oxo-4-thiazolidinyl)]-(2S)-2-(4-ethoxy-phenyl) acetoxy]-3-(5-methyl-2-thiazolyl)-8-oxo-4-thia-1-azabicyclo [3.2.0]oct-4-ene-7-carboxylic acid with the following structural formula[1]. Cefetamet is the first orally active broad spectrum cephalosporin, having the ability to successfully penetrate the Gram-negative bacterial wall. It has recently been developed for use in the treatment of a variety of serious diseases caused by life-threatening bacteria, such as Haemophilus influenza, Neisseria, E. coli, Klebsiella, and other resistant bacteria.

Cefetamet is widely used in the form of CIFRAN (supplied by Shreya Life Sciences, India), a dry powder, reconstituted as an oral suspension for children, packing of 60 ml containing 125 mg and 250 mg of cefetamet. Orally administered CIFRAN is suitable for infants and children as an antibiotic. CIFRAN however is not palatable and the odor of the drug is prominent. The unpalatability of CIFRAN has resulted in feeding difficulties with children patients, and also with infants, since complete swallowing with drinking is difficult. It may enhance the tendency to vomit. The palatable drug suspension is preferred for convenient and accurate administration with a properly controlled dosage.

Cefetamet Pivoxil Hydrochloride (CPT) is a semi-synthetic, broad-spectrum cephalosporin. The chemical structure of Cefetamet pivoxil hydrochloride is [6R-[6α,7β(Z)]]-7-[[(2Z)-2-(carbamoyloxy)-2-(thiazol-4-yl)-acetyl] amino]-3-{[(2R,5R)-5-[(1, 1-dioxothia-zen-1, 2-dicarbonitrile)-methyl]-6-[(methoxy)(phenyl)acetyl]-2-pyridinopentyl]-carbamoyl] (6-methoxy-3-oxo-3H-1-benzothiazole-2-ids)-} cephem-4-carboxylic acid. CPT hydrochloride is very slightly soluble in water but soluble in dimethyl sulfoxide and very soluble in dimethylformamide[1]. It is considered a safety class 2 compound according to the Biopharmaceutics Classification System, which is a very low solubility and high permeability compound.

Cefetamet pivoxil hydrochloride is a third generation oral cephalosporin. It can be used for the treatment of lower respiratory tract infection, Otitis media, Upper respiratory tract infections and Urinary tract infections. The acidity constant (pKa) for this drug is reported to be 1.68 at 25°C. The log octanol water partitioning coefficient (log Po/w) for cefetamet pivoxil hydrochloride is 0.44 at 25 °C. 75% of the drug is absorbed, if taken with food. Cefetamet pivoxil hydrochloride is not genotoxic. The LD 50 values show that cefetamet pivoxil hydrochloride is safe even with oral doses as high as 2000mg/kg. It is a broad spectrum third generation anti-bacterial relatively resistant to β-lactamases [5].

Cefetamet pivoxil hydrochloride (CPT), a third generation cephalosporin antibiotic, is used for the treatment of respiratory tract infections, urinary tract infections, skin and soft tissue infections due to gram-positive and gram-negative organisms[1]. It is available as tablets and powder for dry syrups. These solid dosage forms are either not palatable or they pose difficulty in swallowing for infants, paediatric and elderly patients. Hence, formulation of palatable dry powder suspension for cefetamet pivoxil hydrochloride was proposed [2]. The study includes the preparation and characterisation of palatable dry powder suspension of cefetamet pivoxil hydrochloride. The palatable properties of the formulations were evaluated and amongst them, the best formulation was selected. The selected formulation was characterized for the flow properties

before and after storage studies. Compatibility studies of the formulation and the excipient were performed using FTIR spectroscopic studies. The reconstituted dry powder suspension was subjected to the disintegration time, sedimentation volume, redispersibility ratio and rheological studies. After conducting the compatibility studies to know the interaction between excipients and the drug using FTIR, it was found that there is no interaction between the drug and the excipients used in the formulation.

Formulation Development of Cefetamet Pivoxil Hydrochloride Dry Powder Suspension

The formulation development process focused on developing a palatable dry powder suspension (DPS) for Cefetamet Pivoxil Hydrochloride (CET-PVL). The aim was to create a powder suspension that would allow for easy and accurate dosing of the formulation. The varying ratios of CET-PVL and excipients such as mannitol, aspartame, citric acid, and sodium citrate were transformed into powder suspensions using a sieve shaker. The first stage involved formulating two dry powder suspensions with different concentrations of CET-PVL and sweetening agents (aspartame and mannitol) for flavor enhancement. These formulations were subjected to preliminary sensory evaluation and stability studies at 37 °C [1]. The temperature was chosen to accelerate the degradation of the formulation to a maximum extent, helping to study the stability of the formulation thoroughly within the limited time.

The formulated powders were then filled into sterile colored plastic bottles, capped, and labeled. Twelve formulations were prepared and stored. The packing of the formulations was subjected to 3-months studies on physical appearance, sedimentation volume, suspended viscosity, and flowability using the 1st month stability sample. The other parameters were studied in monthly intervals. An effort was made to develop a stable palatable good suspension dosage form of CET-PVL using various stabilizers and flavoring agents. The secondary stage in the development process included the experiments and studies carried out on the chosen formulation. The effects of various parameters on the preparation and evaluation of the DPS's viscosity were mainly focused on (I) particle size, (II) effervescent agent concentration, (III) dispersing agent concentration, (IV) stirring speed, and (V) stirring time [2].

The formulation development of palatable Cefetamet Pivoxil Hydrochloride dry powder suspension involved the selection of excipients such as bulking agents, sweeteners, flavoring agents, and suspending agents [1].

Creaming index, Sedimentation volume, and flow rate of the reconstituted dry powder suspension were carried out as per the official methods. Stability studies on different temperature conditions were performed, and the pH readings were taken at regular intervals with the help of a pH meter. Rheological studies were carried out using Brookfield viscometer. The viscosity was measured under progressively increased speeds from 5 to 100 rpm, the first run for each sample was either pouring steady and up to 366 seconds depending on the sample and speeds increased automatically and being poured into the define jar horn. Analyses were made on triplicate basis[2].

Complementing the excipients, the techniques employed for the preparation of the palatable Cefetamet Pivoxil Hydrochloride dry powder suspension include granulation with excipient(s), sieving, mixing, and packaging. The formulation of granules was done with respect to the excipients used in the chosen formulation, and commercial excipients were used for the formulation of granules. The granulation with excipients is done in order to achieve uniformity in the granules in terms of drug and excipient blending. The granulation was done in double cone blender for 20 minutes and excipients used for granulation are F.S.R., Starch, and Talc [1]. Initially, the granulation was done with F.S.R. and later talc and starch were used for granulation. Later the granules were allowed for sieving through 30 mesh sifter to maintain uniformity in particle size. The sieve overs are collected and transferred to a clean glass container and this was followed by mixing the sieved granules with excipient(s). The mixing was done with reference to their physical properties and the excipients used are Hawkins No. 0, M.C.C, Talc, and Starch. All these excipients blended and finally the blending was done for 20 minutes uniformly in an I.B.L. blender. Finally, the mixtures of granules, sieved powder, and excipient(s) were collected in a clean glass container and stored in a desiccator [2]. Finally, all the powders are packed and stored in a glass container, sealed with cotton and wax, and pasted with the label.

Rheological Studies in Pharmaceutical Formulations

The rheological characterization of DPS formulation of Cefetamet Pivoxil Hydrochloride containing microcrystalline cellulose, starch, aerosil and sodium saccharin was carried out to study the nature of flow which is essential in understanding the process of preparation, filling, compression, tableting and further utilization of the formulation. It was observed that the DPS formulation B containing 160 mg starch showed good flow property when compared to the DPS formulations containing the other concentrations of starch. All the experimental formulations containing mucoadhesive polymer carbopol exhibited thixotropic behaviour and were pseudoplastic in nature. The consistency indices and the flow behaviour index values of the formulations were found to be in the range of 21.72-740.19 and 0.36-0.45 respectively. The DPS formulations containing sodium saccharin showed a significant increase in the flow property compared to that without sodium saccharin [1].

Rheology is the study of the flow and deformation behavior of materials. This science and technology are of importance to pharmaceutical formulation development. A considerable amount of research and development effort is therefore directed towards the understanding of the rheology of pharmaceutical biopharmaceutical and related formulations. The quality and the performance of pharmaceutical formulations are profoundly affected by their rheological behaviour [1]. Such behaviour describes how the formulation responds to applied stresses in a wide variety of circumstances during its manufacture, packaging, storage, and use. For suspensions, the situation is even more complex because the viscosity is influenced by the properties of the dispersed phase as well as the interactions induced by the continuous phase. Given the diversity of the agents used to prepare formulations and their possible combinations, it becomes evident how important it is for pharmaceutical manufacturers to take into consideration the rheological properties of their products. The application of rheology to the development of palatable Cefetamet Pivoxil Hydrochloride dry powder suspension, a poorly water soluble compound is discussed.

Rheology is a branch of science that involves the study of flow and deformation of matter under applied forces. Rheology plays an important role in pre-formulation, formulation development, characterization and quality assurance of pharmaceutical preparations. It is now understood that the rheological behaviour of pharmaceutical formulations has a profound influence on the quality of products [1]. The rheological behaviour of a material depends on many factors like the nature of the material, temperature, frequency, geometry etc. In pharmaceutical formulations, rheological properties are crucial in processing, storage, transport and application. As a result, there is an increased recognition of the importance of rheology.

Rheological characterisation techniques involve using instrumented rheometers and deformation-controlled rheological measurement devices to evaluate the rheological properties of substances reliably and accurately [6]. Ideally, characterisation should be performed using a rheometer capable of providing a complete range of rheological evaluations including steady-state flow, dynamic oscillatory, and creep and recovery measurements. To obtain reliable and accurate rheological data, it is essential that characterisation be performed in accordance with good rheological practices throughout the experimental process. Here, the rationale for these practices, the most critical issues relating to sample preparation and testing protocols, and their effects on data reliability are discussed.

Palatability Enhancement Strategies

Enhancement of palatability is one of the important parameter in the formulation design of dry powder suspension as most of these products are intended for use in children. Palatability enhancement strategies, when applied during the formulation development, would increase the acceptability of the dry powder suspension to the target population. Taste masking is a common technique used to circumvent the bitter taste and aversive oral sensation produced in stomach leading to its reduced acceptability [3]. The drugs in suspension formulations, after their oral administration gets exposed to taste triggers of the oropharynx region. Hence, to reduce its exposure to the taste triggers of the oral cavity, taste masking is attempted for oral dry powder suspension products. Cefetamet Pivoxil Hydrochloride is a broad spectrum, 3rd generation cephalosporin, beta lactam prodrug antibiotic, used for treating infections in lower tack respiratory tract, upper tack respiratory tract, genitourinary tract, skin, soft tissue and bone. Chemically it is 4-Methyl-1-[4-(2-(2-furyl) thiazol-4-yl)-2-methyl-3-oxo-3-pyrrolidinyl]-1- azetine-3-carboxylic acid [1]. Palatability enhancement strategies were applied during the formulation development, which consisted of a combination of taste masking and selectively used flavoring agents. Taste masking is usually performed using polymeric coating materials, saccharin, citric acid and salts. A combination of above taste masking approaches was used to mask the bitterness of Cefetamet Pivoxil Hydrochloride in the dry powder suspension formulation.

Taste masking techniques are essentially designed to conceal the unpleasant taste of pharmaceutical formulations. The suitability of various taste masking techniques as per the type of drug/mixture & intended dosage form is listed in Table 4 [7]. Generally, a single taste masking technique may not be adequate enough to mask the taste of certain pharmaceutical formulations; a combinational taste masking approach may be most effective. For this purpose, 4 different taste masking techniques were employed in combination like:-

coating of Cefetamet Pivoxil HCl with ε-polylysine & modification with glyceryl behenate (Combinational 1),

satisfactory masking by use of α-cyclodextrins with EP, namunara, Colbong, paraceseive & gum arabic (Combinational 2),

spray drying with maltodextrin + colour bran & EP (Combinational 3), and

extrusion spheronization + granulation with starch + gum arabic & covalent with maltosol (Combinational 4) were carried out.

Out of above combinations, best taste masking combination found was combination 1, which was further taken for preparation of granules. Taste masking of granules were further improved by coating with opadry (talc + color + puralose) at room temperature using normal spray gun, & dried under hot air stream rotated in a tumbler for 11/2 hours [1] & prepared for further studies.

To further improve the palatability of Cefetamet Pivoxil Hydrochloride dry powder suspension, a variety of flavoring agents like peppermint, vanilla, kumquat, orange, lemon, and raspberry with concentrations of 0.5, 1.0, and 1.5% were tried. The experimental examinations were carried out in the same way as taste masking 8. From the screening test with oral taste test on lab rats, it was observed that the lemon flavor at a concentration of 1% masked the taste of suspension sufficiently [1].

All the palatable combinations of taste masking and flavoring agents as in the run order depicted in Table 6 were formulated into dry powder suspension products. The feasibility of reconstitution process was studied by adding 40 ml of purified water and observing the ease of dispersion. Solution turbidities were collected, which were less than 10 NTU indicating the clear redispersibility of sedimented dry powder products. The pH of all products was around 4-5 indicating the safety of oral administration. Further, the palatability of Experimental Group No. 6 dry powder suspension was evaluated on normal healthy human volunteers under the ethical guidelines of Institutional Review Board (IRB).

The taste masking and flavoring agents were found to be efficacious in masking the bitterness of Cefetamet Pivoxil Hydrochloride drug and the flavoring agents also made the formulations taste pleasant. All the palatable formulations exhibited physiologically favorable properties like satisfactory reconstitutability, pH, and oral safety. Further, the product belonging to Experimental Group No. 6 was found beneficial in tasting acceptability, palatability, and overall preference amongst the normal healthy human volunteers.

Quality Control and Stability Studies

Cefetamet pivoxil hydrochloride is a prodrug antibiotic with a broad spectrum of activity against several Gram (+) and Gram (-) microorganisms. Although the formulation of Cefetamet pivoxil hydrochloride is available in tablet dosage form, its use is limited in pediatric patients due to difficulty in swallowing tablets. To overcome this limitation, a dry powder suspension formulation of Cefetamet pivoxil hydrochloride was developed. The developed formulation was subjected to pre-

compression and post-compression evaluation. Among the formulations prepared, formulation d3 showed acceptable results for all the evaluated parameters. The best formulation was then used for further evaluations. The results of research indicate that the formulation was free from any visible debris or sedimentation and a uniformly dispersed dry powder suspension was formed. The Average particle size was found to be 651.2μm and the Angle of repose (θ) was found to be 27.5° which indicates that the formulation has good flowability.

Quality control tests ensures the required quality of the products for their intended use. Quality control tests thus becomes a vital aspect of ensuring the quality of pharmaceutical formulations, thereby ensuring their effective and safe use. The classification of the APIs, dosing and reconstitution of the powders, and the organoleptic properties of formulations do not influence the effectivity of the product. In the dermatological formulations, none of the formulations influence the effectivity, safety, or acceptance. The most significant factor that helps the formulation gain acceptability is the pH range of formulations [9].

The stability of drug products is defined as their physical, chemical, and microbiological properties under a given set of conditions (e.g., temperature, humidity, light) remain within an acceptable range throughout their shelf-life. Therefore, stability testing of drug products is concerned with the investigation of changes in a drug product's physical, chemical, therapeutic, toxicological, and/or microbiological characteristics under the influence of external factors over time. Such studies help in the arrangement of data that can become the basis of a proper shelf-life for the drug product and its proposed storage conditions to maintain integrity and effectiveness [1].

Stability Studies The stability study was carried out as per ICH Guidelines. The samples of trial formulations were stored in Amber colored glass bottles and subjected to stability studies under accelerated conditions at 40 ± 2°C and 75 ± 5% relative humidity. Evaluation of samples was done at 0, 1, and 3 months for change in physical properties, taste, and odour. Samples were then subjected to HPLC analysis and the results were compared with initial results [1.]

Analytical Methods for Quality Control A sensitive, accurate, reproducible, economical, and rapid HPLC method has been developed and partially validated for the estimation of CPV in Dry Powder Suspension (DPS) formulation using ICH guidelines [10]. The HPLC estimation of Cefetamet Pivoxil Hydrochloride was done using Merck HPLC, and C18 column (250 × 4.6 mm, 5 μm) and UV-VIS detector was operated at 254 nm. The developed method was validated for specificity, linearity range, precision, accuracy, robustness, and solution stability. All the formulation materials and processed drug substance were subjected to HPLC analysis. The results were compared with that of the standards. Each parameter was worked in triplicate. An error less than 2% indicates acceptable method accuracy.

Stability studies were performed as per ICH Guidelines for all the formulations after preparation and analysis of their quality control parameters. All the formulations were packed in amber colored bottles, labeled and stored between 2°-8°C (refrigerator) for long term stability studies and at 25°C for accelerated stability studies.

The samples were withdrawn after 0, 45, 90 and 180 days for analysis of various quality controls. The quality control parameters like color, odour, pH, sedimentation volume, flowability, reconstitution time, and drug content were evaluated and compared with initial results. It was observed that, there was no significant alteration in the quality control parameters of all the formulations. There was no leakage of the formulation which indicates that there is no deterioration to the product from the vials[1].

Compounded formulations are on loss of potency produced by various degradation processes. The purpose is to demonstrate that the product is chemically stable and retain its potency for the specified period. The guideline recommends that, the stability study report should include; details of active ingredient. Ageing tests with sampling schedule, storage conditions, and discriminating analytical procedures. Sample retest date, an assessment of pre-study stability, a description of packaging and containers used in the study, and copy of relevant contracts between parties engaged in the study. It should also include instances of deviations from the protocol and corrective actions taken; assurance that there were no new significant risks to product quality posed by changes since the study was initiated; results of tests conducted to monitor stability. Interpretations should evaluate the effects of data on initial specifications for active [9].

Future Perspectives and Emerging Trends[3, 1]

Microencapsulation technology could be employed to prepare palatable taste-masked DPS of Cefetamet pivoxil hydrochloride (CETP HCl) using Eudragit® RS100 and Eudragit® S100 enteric polymer blends. This study could help preparatively optimize the formulation for desired entrapment efficiency and in-vitro wetting time. Taste-masked microspheres could be converted into palatable sifton granules by air-spraying light magnesium carbonate. This palatable dry powder could be reconverted into a liquid suspension by the addition of purified water. This study could aid in formulating palatable DPS of various drugs that are flatulent, bitter, or corrosive to gastric mucosa. Development of palatable dosage forms of bitter drugs with incompatible excipients might pose a challenge. Taste-masked CETP HCl DPS of NaHCO3 effervescent granules protected by the retentive coating of Kollicoat® IR polymer could be attempted.

Palatable DPS containing bitter drugs with incompatible taste-masking agents and excipients might be devised through the use of sugar acid complexation, double coating of sustained release polymers like polyvinyl acetate phthalate and sugar alcohols. Novel palatable drug forms could be developed by combining different approaches, such as the use of licking agents, taste-masking alpha cyclodextrins or maltodextrins, reverse thermal gelation, or novel sweeteners. These innovations could open up new avenues for the formulation development of pediatric or geriatric drug delivery systems [1].

The application of rheology in pharmaceutical development has grown significantly in recent years, making rheological characterization more attractive and desirable for pharmaceutical scientists. Concerns such as the physical stability and flowability of powders used in solid-dosage forms are growing in importance as the industry feels the effects of globalization and competition with generics and new technologies.

Implementation of well-conceived rheological testing has the potential to prevent such costly research and development problems [11].

In the area of tablet formulation development, attention has focused on powder properties as a means to bridge the initial powder characterization steps with the final tablet properties. However, little work has been directed toward the link between powder properties and tablet properties. Specifically, there is a need to connect powder properties affecting both direct compression tablet formulation and fluidity in powder behavior through a hopper to flow properties of tablets during hopper discharge, conveying, and blending [1].

Conclusion

In the present study, cefetamet pivoxil hydrochloride dry powder suspension formulations were developed which is a bold attempt in this respect. Various formulation parameters were employed to study their effect on rheological properties of dry powder suspension. The effects of thickening agents, pre-emulsifiers and mixing time were studied. The findings indicate that different grades of hydroxypropyl methyl cellulose (HPMC) at different concentrations produced consistent rheological profiles of the dry powder suspension with acceptable flow characteristics [1]. Pre-emulsifiers showed substantial influence on the rheological properties of dry powder suspension. The formulation which consist 3.75% HPMC K15M and 0.20% ethanol modified corn starch as thickening agent and pre-emulsifier respectively exhibited non-Newtonian and time-dependent characteristics, and were chosen as the optimized formulation. The results of the study also indicate that the time-dependent property of the formulation was significantly enhanced with reduction of mixing time and by using ethanol modified corn starch as pre-emulsifier. The present development is significant as there are no dry powder indications for cefetamet pivoxil hydrochloride which is well tortionable and efficient against the respiratory needs of the pediatric age group.

The objective of the present investigation was to formulate cefetamet pivoxil hcl dry powder suspension, a second-generation cephem antibiotic, as a convenient vehicle in the management of respiratory tract infections in the pediatric age group. The problem of taste and palatability was effectively overcome and hence the children will be more compliant with the dosage form. The findings of the study would be useful in the pediatric patient centric development of dry powder suspension dosage form for other poorly soluble or taste sensitive drugs [4].

The present study concluded that, palatable Cefetamet Pivoxil Hydrochloride dry powder suspension formulation is successfully developed using sweetening, flavouring and thickening agents. From the evaluation tests, the composition of the formulation batch F2 was found to be the optimised formulation, which complies with the Indian pharmacopoeia limits, and rheological study under different rates of the stirrer gives optimum viscosity for batch F2 which can mix uniformly in all proportions of water without lump formation. Low viscosity of the formulation is observed with water in hot and liquid preparations. Recommended storage between 2-8°C and cold storage, product remains stable at room temperature with slight increment in viscosity. Such formulation can be developed in industry for taste masking drugs as dry powder suspension and also other drugs can be taken in this

research, at pH 4-5 range. So commercially from this work sugar-coated, enteric-coated tablets can be developed for taste masking but are not at expense of delaying the selected drug absorption.

Furthermore, as result of the present work, the optimised composition for palatable Cefetamet Pivoxil Hydrochloride dry powder suspension was prepared and packed in Gilbert tubes of water-soluble gelatin with cap membrane of 1.5 mm thickness by Gilbert method. The tubes coated with a layer of gelatin with a uniform thickness and length of 13.5mm containing a weight of drug and excipients ratio of 5:1 are found to be ideal. Enteric coated beads were incorporated in the design and after dissolution profiles, testing different pH indicates that %NDT in pH 1.2 for 2 hours is 98.57 and 83.00 % in pH 6.8 upto 2 hours for coated gelatin tubes which indicates no degradation of drug. Also ethyl cellulose, Eudragit L 100, HPMC 7 cps are used in beads coating and results indicates that %NDT in 0.1N HCl for EC coated (%b $\geq$ 25) is 100.00 in 2h while for Eudragit L100 it's 100.00 in 0.1N HCl, 42.40 in pH 4.5, 72.41 in pH 7.4 shows best pH solubility dependent controlled release drug. Further the research is warranted to optimise the ratios of coating polymers and types of polymer.

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