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Formulation and Characterization of Patient-Friendly Dosage Form of Ondansetron Hydrochloride

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ABSTRACT

Ondansetron hydrochloride is an intensely bitter antiemetic drug used to treat nausea and vomiting following chemotherapy. The purpose of the present work was to mask the taste of ondansetron hydrochloride and to formulate its patient-friendly dosage form. Complexation technique using indion 234 (polycyclic potassium with carboxylic functionality) and an ion-exchange resin was used to mask the bitter taste and then the taste-masked drug was formulated into an orodispersible tablet (ODT). The drug loading onto the ion-exchange resin was optimized for mixing time, activation, effect of pH, mode of mixing, ratio of drug to resin and temperature. The resinate was evaluated for taste masking and characterized by X-ray diffraction study and infrared spectroscopy. ODTs were formulated using the drug–resin complex. The developed tablets were evaluated for hardness, friability, drug content, weight variation, content uniformity, friability, water absorption ratio, *in vitro* and *in vivo* disintegration time and in vitro drug release. The tablets disintegrated in vitro and in vivo within 24 and 27 s, respectively. Drug release from the tablet was completed within 2 min. The obtained results revealed that ondansetron HCl has been successfully taste masked and formulated into an ODT as a suitable alternative to the conventional tablets.

Key words: Indion 234, taste masking, sodium starch glycolate, ondansetron hydrochloride, orodispersible tablet

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INTRODUCTION

Convenience of administration and patient compliance are gaining significant importance in the design of dosage forms. Recently, more stress is laid down on the development of an organoleptically elegant and patient-friendly drug delivery system for pediatric and geriatric patients.[1,2] More than 50% of the pharmaceutical products are orally administered for several reasons, and undesirable taste is one of the important formulation problems encountered with such oral products. Taste of a pharmaceutical product is an important parameter for governing compliance. Thus, taste masking of oral pharmaceuticals has become an important tool to improve patient compliance and the quality of treatment, especially in pediatrics. Therefore, formulation of taste-masked products is a challenge to the pharmacists.[3,4]

Ondansetron HCl is a potent antiemetic drug indicated for the treatment and/or prophylaxis of postoperative or chemotherapy- or radiotherapy-induced emesis, and is also used in the early onset of alcoholism.[5] In general, emesis is preceded with nausea and, in such a condition, it is difficult to the administer drug with a glass of water. Hence, it is beneficial to administer such drugs as orodispersible tablets (ODTs). Ondansetron HCl is an intensely bitter drug; hence, if it is incorporated directly into an ODT, the main objective behind formulation of such a dosage form will definitely be futile.[6] Thus, in the present study, an attempt has been made to mask the taste of ondansetron HCl and

to formulate ODTs with a good mouth feel so as to prepare a "patient-friendly dosage form."

Mouth-dissolving tablets are dosage forms that disintegrate in patient's mouth within a few seconds without the need of water, or chewing, providing best remedy for patients suffering from dysphagia. Their growing importance was underlined recently when the European pharmacopoeia adopted the term "orodispersible tablet" as a tablet that is to be placed in the mouth where it disperses rapidly before swallowing.[7]

Ion-exchange resins have been increasingly used as taste-masking agents. They are also known to be useful as disintegrating agents.[8,9] Thus, the study undertaken was aimed at using ion-exchange resins for both the purposes, formulating taste-masked ODTs of ondansetron HCl.

The complex of cationic drug and weak ion-exchange resin does not break at the pH of saliva, i.e. 6–7, with a cation concentration of 40 meq/l. But, at the high cationic concentration in the stomach and pH 1.2, free drug is immediately released. This implies that while passing through the mouth, the drug remains in the complex form, thereby imparting no bitter taste in the mouth. This property was exploited to formulate the "consumer-friendly dosage form," i.e. mouth-dissolving tablets.[10]

MATERIALS AND METHODS

Materials

Ondansetron HCl was a gift sample from Alkem Laboratories (Mumbai, India). Indion 234 was obtained from Ion Exchange India Ltd., Mumbai, India. Starlac and MCC (PH 101) were provided by Signet Chemicals Ltd., Mumbai, India. All other chemicals and reagents used were of high analytical grade.

Methods

Preparation of drug–resin complex (resinate)
Resinate were prepared using the batch method.[11] Water is used as a medium for complexation because the drug is soluble in water.[12] An accurately weighed amount of resin (100 mg) was placed in a beaker containing 50 ml of deionised water. Accurately weighed 100 mg of ondansetron hydrochloride was added to the resin solution and stirred for 180 min. The mixture was filtered through a Whatman filter paper and the residue was washed with 50 ml of deionised water to remove any uncomplexed drug. Unbound drug in the filtrate was estimated at 310 nm and the drug-loading efficiency was calculated.

Optimization of Ondansetron HCl–indion resin complexation
The drug loading on to the resin was optimized for various parameters such as mixing time, activation, effect of pH, mode of mixing, ratio of drug:resin and effect of temperature.

Optimization for mixing time on drug loading
Separate batches of indion 234 (100 mg) were soaked in 50 ml of distilled water in a beaker and about 100 mg of drug was added and stirred for 3 h. The mixture was filtered through a Whatman filter paper and the residue was washed with 50 ml of deionized water to remove any uncomplexed drug. Unbound drug in the filtrate was estimated at 310 nm and the time required for maximum adsorption of the drug was optimized.

Effect of activation of resin on drug loading
Resins were washed with distilled water and subsequently with 1 N HCl. The resins were rewashed with water until neutral pH was reached. Drug:resin complexes were prepared by placing 100 mg of acid-activated resins in a beaker containing 50 ml distilled water and about 100 mg of drug and stirred for 3 h, and the drug content was determined as mentioned previously. Similarly, alkali activation of indion 234 was performed, replacing 1 N HCl with 1 N NaOH.

Effect of pH, mode of mixing, ratio of drug:resin and temperature on drug loading
For optimization of pH, weighed, 100 mg of drug was added to 100 mg of activated resins in 50 ml of distilled water. The pH of the solutions was adjusted at 3.0, 3.5, 4.0, 4.5, 5.0, 5.5, 6.0 and 6.5 and stirred for 3 h and the drug content was determined as mentioned previously.[11] For optimization of mode of mixing, rotary shaker and magnetic stirrer were used. For all activated resins (100 mg) in 50 ml of distilled water and about 100 mg of drug, the pH was adjusted at 3.5 and the drug content was determined as mentioned previously. For optimization of ratio of drug:resin, three batches were prepared containing drug–resin in the ratio of 1:1, 1:2 and 1:3. The pH was maintained at 3.5. The solution was stirred using a magnetic stirrer for 3 h. To study the effect of temperature, separate batches were prepared containing drug–resin in the ratio of 1:3. The pH was maintained at 3.5 and was stirred using a magnetic stirrer at 30°, 35°, 40°, 50° and 60°C and the drug content was determined as mentioned previously.

Characterization of resinate
FT-IR spectrum of the drug, resin and resinate were