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ORIGINAL ARTICLE

Formulation and evaluation of orodispersible tablet of taste masked doxylamine succinate using ion exchange resin

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Abstract Doxilamine orodispersible tablets were developed with considerable increase in drug release as compared to marketed formulations, seven formulations were developed and studied. The difference in drug release values was found to be 100.45 ± 1.89 and 56.47 ± 1.89, respectively. To prevent bitter taste and unacceptable odour of the drug, the drug was taste masked with weak cation exchange resins like Indion 234, Indion 204 and Indion 414. The drug was characterized according to different compendial methods, on the basis of identification by UV spectroscopy, pH, organoleptic properties and other tests. Among the three resins, one was selected for further studies i.e., Indion 234, because of high drug loading capacity. Drug–resin complex was prepared using batch method and effect of various processing parameters viz. drug–resin ratio, pH, temperature and drug concentration was studied to optimize the loading conditions. Maximum loading was obtained at drug–resin ratio 1:2, pH 5, temperature 50 °C and drug concentration 4 mg/ml. A successful taste masking of resinate was confirmed by time intensity method and also by taking drug release in 0.01 N hydrochloric acid and in simulated salivary fluid. The values of pre-compression parameters evaluated, were within prescribed limits and indicated good free flowing properties. The data obtained of post-compression parameters such as weight variation, hardness, friability, wetting time, water absorption ratio, content uniformity, disintegration time and dissolution and was found superior over conventional formulation. The F5 batch with disintegration time 25.24 ± 0.75 and dissolution 100.46% ± 3.78 was selected as optimized formulation. This was compared with conventional marketed formulation and was found superior. Batch F5 was also subjected to stability studies for three months and was tested for its disintegration time, drug contents

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and dissolution behaviour monthly. It was observed that the contents of the tablets remained the same. By an appropriate selection and combination of excipients it was possible to obtain orodispersible and taste masked tablets.

1. Introduction

The term 'Orodispersible Tablet' as appears in European Pharmacopoeia (Suppl. 4.1, IV Ed.) is defined as ''uncovered tablet for buccal cavity, where it disperses before ingestion''. They obviate the problem associated with conventional dosage forms, it has benefits like desired hardness, dosage uniformity, extremely easy administration and since no water is required for swallowing these tablets are suitable for geriatric, paediatric and travelling patients. These tablets display a fast and spontaneous de-aggregation in the mouth, soon after it comes in contact with saliva, dissolving the active ingredient and allowing absorption through all possible membrane it comes in contact during deglutition (Sharma et al., 2008).

In the recent past, several new advanced technologies have been introduced for the formulation of orodispersible tablets with very interesting features, like extremely low disintegration time, exceptional taste masking ability, pleasant mouth feel and sugar free tablets for diabetic patients (Shukla et al., 2009). The technologies utilized for fabrication of orodispersible tablets include lyophilization (Virely and Yarwood, 1990), moulding (Pebley et al., 1994), direct compression (Watanabe, 1995), cotton candy process (Myers et al., 1995), spray drying (Allen and Wang, 1996), sublimation (Koizumi et al., 1997), mass extrusion (Bhaskaran and Narmada, 2002), nanonization (Khan et al., 2007) and quick dissolve film formation (Khan et al., 2007). These techniques are based on the principles of increasing porosity and/or addition of superdisintegrants and water soluble excipients in the tablets (Biradar et al., 2006). The formulations prepared from these techniques differ from each other on the basis of the factors like mechanical strength of final product, drug and dosage form stability, mouth feel, taste, rate of dissolution of the formulation in saliva, rate of absorption from saliva and overall drug bioavailability and polymers (Kuchekar et al., 2003). Taste masking of the drug employing ion exchange resins (IER) has proved to be safe and effective method for formulation of various dosage forms.

In this paper we report the formulation and evaluation of orodispersible tablet of taste masked doxylamine succinate. Doxylamine succinate is an antihistaminic commonly used to prevent morning sickness in pregnant women. It is an extremely bitter drug therefore it is very essential to mask the bitter taste. It's formulation into simple tablet may induce vomiting, but formulation of taste masked doxylamine succinate in orodispersible tablet will give rapid action and will prevent morning sickness. Taste masking by ion exchange resin i.e., Indion 234 was employed because of its better drug loading and taste masking. Ion exchange resins have been increasingly used for the taste masking of bitter taste drug and help to prepare orodispersible tablets (Nandgude et al., 2007).

Ion exchange resins are solid and suitable in solubilised high molecular weight polyelectrolytes that can exchange their mobile ions of equal charge with the surrounding medium reversibly and stotiometrically. They are available in desired size ranges. Bitter cationic drugs can get adsorbed on to the weak cationic exchange resins of carboxylic acid functionally to form the complex which is not bitter. Further resinates can be formulated as lozenges, chewing gum, suspension or dispersible tablet and mask the taste (Rishi, 2004). Drug can be bound to the resin with the drug solution. Drugs are attached to the oppositely charged resin substrate or resonate through weak ionic bonding so that dissociation of the drug–resin complex does not occur under salivary pH conditions. This suitably masks the unpleasant taste and odour of drugs (Kaushik et al., 2004).

Taste is an important parameter in administering drugs orally. Undesirable taste is one of the important formulation problems that are encountered with many drugs. Administration of bitter drugs orally with acceptable level of palatability is a key issue for health providers. Proven methods for bitterness reduction and inhibition have resulted in improved palatability of oral pharmaceuticals (jeong et al., 2005). Taste masking is an essential requirement for fast dissolving tablets for commercial success. Taste masking of the active ingredient can be achieved by various techniques. Drugs with unacceptable bitter taste can be microencapsulated, such as Cefuroxime axetil can be microencapsulated in various types of acrylic polymers, Beclamide can be coacervated using gelatin. Macrolide antibiotics are having unacceptable taste (erythromycin and clarithromycin; Yajima et al., 1999) has reported successful taste masking using monoglycrides.

2. Materials and methods

2.1. Materials

All materials used in the present research were commercial samples. *Active agent*: Doxylamine succinate (Adroit Pharmaceuticals Pvt. Ltd., India), Pyridoxine HCL (Adroit Pharmaceuticals Pvt. Ltd., India); *ION Exchange Resins*: Indion 204, Indion 234 and Indion 414 (ION Exchange India Ltd., Mumbai, India); *Excipients*: VIVAPUR 102 (Microcrystalline Cellulose NF, Ph. Eur., JP), VIVASOL (Croscarmellose Sodium Ph. Eur., NF. JPE), VIVASTAR® P (Sodium Starch Glycolate, Ph. Eur.), Avicel PH 113 (Microcrystalline Cellulose USP/NF, EP,JP), Kollidon CL-SF (Super Fine Grade Crosspovidone USP/NF, EP, JPE), Lactopress® Anhydrous 250 (β-Lactose anhydrous USP/NF, EP, JP) and Ac–Di–Sol (Croscarmellose Sodium, NF, Ph, Eur., JPE) were gift by JRS PHARMA GmBH & CO. KG 73494, Rosenberg, Germany.

2.2. Preparation of tablets

The preparation of tablets was carried out after the analysis of drug samples, ion exchange resins, mixture formation and their