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Formulation and Evaluation of Oral Fast Dissolving Tablets of Promethazine HCl by Sublimation Method

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Abstract: Fast dissolving drug delivery systems have gained patient acceptability and popularity in the recent times. The purpose of this work was to develop oral fast dissolving tablets of Promethazine HCl. Promethazine is an antiemetic drug especially used for motion sickness condition. Promethazine undergoes first pass metabolism in liver hence oral bioavailability (88%) was reduced to 27%. Hence an attempt has been made to prepare fast dissolving tablets by direct compression method using camphor as subliming agent in three concentrations of 2%, 5% and 10%. Sodium starch glycolate, crosscarmellose and tulsion 414 are used as superdisintegrants in different ratios (5%, 10%). All prepared formulations were evaluated for weight variation, hardness, friability, drug content, disintegration time, wetting time and *in vitro* dissolution. All the formulations showed low weight variation with disintegration time of less than 60 seconds. The results revealed that tablets containing camphor had a good dissolution profile. Among them formulation containing 10%w/w of sodium starch glycolate with 10%w/w of camphor (F6) was known to show 93% drug release within 10 minutes with disintegration time of 26 seconds.
Keywords: Fast dissolving tablets, Promethazine HCl, Sublimation, Tulsion 414, Direct compression.

Introduction

Oral routes of drug administration have wide acceptance up to 50-60% of total dosage forms. Solid dosage forms are popular because of ease of administration, accurate dosage, self medication, pain avoidance and most importantly the patient compliance. The most popular solid dosage forms are being tablets and capsules; one important drawback of this dosage forms for some patients, is the difficulty to swallow. Drinking water plays an important role in the swallowing of oral dosage forms. Difficulty in swallowing tablet is a common problem of all age groups, especially elderly and paediarics, because of physiologic changes associated with these groups of patients. Many patients feel difficulty in swallowing conventional tablets when water is not available, in the case of the motion sickness (kinetosis) and sudden episodes of coughing during the common cold, allergic condition and bronchitis. For these reason, tablets that can rapidly dissolve or disintegrate in the oral cavity have attracted a great deal of attention. Orodispersible tablets are not only indicated for people who have swallowing difficulties, but also are ideal for active people. Fast dissolving tablets are also called as mouth-dissolving tablets, melt-in mouth tablets, Orodispersible tablets, rapimelts, porous tablets, rapid dissolving tablets, quick dissolving tablets, etc., [1-3]
The united states of food and drug administration center for drug evaluation and research (FDA) defines, in the 'orange book', an ODT as "a solid dosage form containing medicinal substances, which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue"[4]. The significance of these dosage forms is highlighted by the adoption of the term, "Orodispersible tablet", by the European

pharmacopoeia which describes it as a tablet that can be placed in oral cavity where it disperses rapidly before swallowing.[5]

Promethazine hydrochloride is a first generation H1 receptor antagonist used medically as an antihistamine and antiemetic. It is chemically (RS)-dimethyl [1-methyl-2-(phenothiazone-10-yl) ethyl] amine hydrochloride is an effective and well tolerated antiemetic that has been associated with a wide variety of chemotherapy and radiotherapy regimens.[6]

The objective of the present work was to prepare fast dissolving tablets of promethazine hydrochloride using camphor as subliming agent with different superdisintegrants to enhance the onset of action of drug.

Materials and Methods

Promethazine HCl was obtained as gift sample from Mayer Healthcare Pharmaceuticals, Bangalore. Sodium starch glycolate, crosscarmellose obtained from Signet chemical corporation, Mumbai and tulsion 414 from Thermax limited, Pune. Camphor, talc, magnesium state, mannitol and sodium saccharine were obtained from Loba chem. Pvt. Ltd, Mumbai. All the ingredients used were of analytical grade.

Methods

The fast dissolving tablets of Promethazine HCl were prepared using camphor as subliming agent in three different proportions of 2%, 5% and 10%. Sodium starch glycolate, crosscarmellose and tulsion 414 as superdisintegrants. Each of the superdisintegrants were used in two different concentrations of 5% and 10%. Mannitol is used as diluents in quantity sufficient; talc is used as flow promoter and magnesium state as lubricant. Sodium saccharine is used as sweetener and raspberry flavour is used for good mouth feel. All the ingredients were passed through mesh screen no. 60 and weighed in geometrical order. All the materials were directly compressible so this uniformly mixed blend was compressed into tablets using single tablet punching machine (CMS15, cadmach). Sublimation was performed from tablets by keeping in hot air oven at 60ºC for 1 hour. Six formulations were prepared. The composition of formulations is shown in Table 1.

Evaluation of tablets

1. Thickness:

The thickness of tablets was determined by using digital caliper. Five trials for each formulation was made.[7]

2. Hardness:

The tablet hardness, which is the force required to break a tablet was measured by using Pfizer hardness tester. Five trials for each formulation were performed.[7]

3. Friability:

Ten tablets were weighed and placed in a Roche friabilator and it is rotated for 4 min. at 25 rpm. The tablets were taken out, dedusted and reweighed. The standard limit of friability is 0.5-1%.

4. Weight variation:

Randomly, twenty tablets were selected after compression and the mean weight was determined. None of tablets deviated from the average weight by more than ±10.5 (USPXX).[8]

5. Drug content:

Twenty tablets were weighed and powdered. An amount of powder equivalent to 150 mg of promethazine hydrochloride was dissolved in 100ml of pH 7.4 phosphate buffer, filtered, diluted suitably and analyzed for drug content at 249 nm using UV-Visible spectrophotometer.[8]

6. *In vitro* dispersion time:

In vitro dispersion time was measured by dropping a tablet in a Petridish containing 10 ml of saliva fluid (pH 7.4). Three trials for each formulation were made.

7. Wetting time:

A piece of tissue paper folded twice was placed in a small petridish (ID=6.5cm) containing 6 ml of simulated saliva pH 7.4, a tablet was put on the paper, and the time for complete wetting was measured. Three trials for each formulation was performed.[9]

8. *In vitro* drug release:

In vitro dissolution study was performed by using USP Type II Apparatus (Paddle type) at 50 rpm. Phosphate buffer of pH 7.4, 900 ml was used as dissolution medium which is maintained at 37±0.5ºC. Aliquot of dissolution medium (5ml) was withdrawn at specific time intervals and was filtered. The same volume of dissolution medium is replaced to maintain sink condition. The absorbance of these aliquots was measured at 249 nm using UV-Visible spectrophotometer (Shimadzu). Cumulative percentage release of drug was calculated using an equation obtained from a standard curve[10].

Table 1: Formulation composition of Fast dissolving tablets of Promethazine HCl

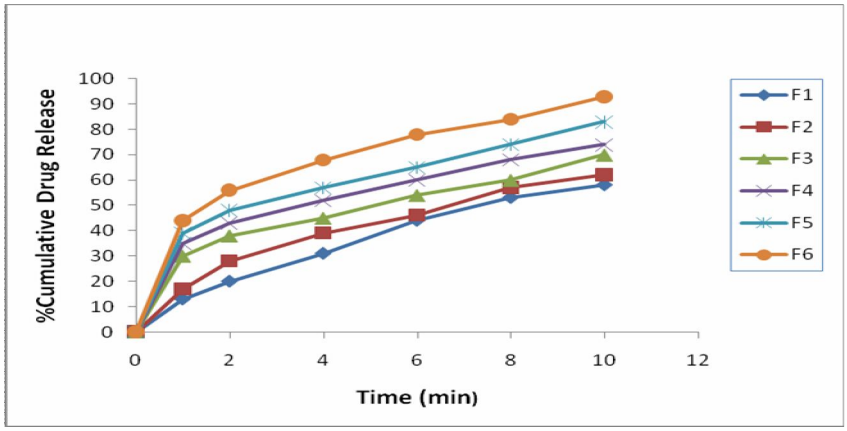
Ingredients(mg)	F1	F2	F3	F4	F5	F6
Promethazine HCl	25	25	25	25	25	25
Camphor	3	3	7.5	7.5	15	15
Crosscarmellose	-	7.5	-	15	-	-
Tulsion 414	7.5	-	15	-	-	-
Sodium starch glycolate	-	-	-	-	7.5	15
Sodium saccharin	3	3	3	3	3	3
Raspberry flavour	2	2	2	2	2	2
Talc	2	2	2	2	2	2
Magnesium state	1	1	1	1	1	1
Mannitol(q.s.)	150	150	150	150	150	150

Table 2: Evaluation parameters of Fast dissolving tablets of Promethazine HCl tablets

Parameters	F1	F2	F3	F4	F5	F6
Thickness	2.6±0.01	2.6±0.07	2.8±0.02	2.6±0.05	2.5±0.01	2.5±0.05
Hardness*	4.8±0.16	4.3±0.32	4±0.56	3.8±1.4	3.4±0.63	3.1±0.78
Friability (%)	0.68	0.58	0.50	0.49	0.45	0.40
Weight variation	151.4±0.1	149±0.45	150.2±0.2	151±0.51	149.5±0.7	150.6±0.2
Drug content (%)	98.4±0.69	97.6±0.8	98.7±0.87	97.6±0.8	98.8±0.64	99.2±0.75
***In vitro* dispersion time**(sec)**	55±2.0	52±3.0	50±3.0	42±2.8	34±4.58	26±1.52
Wetting time(sec)**	82±2.61	76±4.16	70±3.0	64±3.11	54±1.52	40±2.08

*All values of each formulation is expressed as mean ± SD, n=5
**All values of each formulation is expressed as an mean ± SD, n=3

Fig 1: *In vitro* dissolution profile of Promethazine HCl fast dissolving tablets



Results and Discussion

The tablets were prepared by two methods i.e. sublimation and Superdisintegrants addition. Six formulations of Promethazine HCl were prepared with different concentrations of three individual superdisintegrants, crosscarmellose, tulsion 414 and camphor is used as subliming agent. The evaluation parameters of all formulations were given in Table 2.

The drug content was found to be within the range of 97.6 to 99.2 indicating uniform distribution of drug in the formulated tablets as per pharmacopial specification. The hardness of tablets was found to be 3.1±0.78 to 4.8±0.32 which indicates good mechanical strength with an ability to withstand physical and mechanical stress conditions while handling. The decreased hardness of tablets shows less *in vitro* dispersion time (F5, F6).

The wetting time of the formulations was in the range of 45±2.08 to 80±2.61. The wetting time was decreased increasing the concentration of camphor. This may be due to formation of pores in formulations on increasing concentration of volatilizing agent. Similar results were obtained on increasing the concentration of tulsion 414 and crosscarmellose in formulations F1-F4. *In vitro* dispersion time was found to be 26-55 seconds, which may be attributed to faster uptake of water due to porous structure formed. The *in vitro* drug release of all the formulations (Fig.1) was made for maximum time period of 10 minutes.

The formulations (F5, F6) prepared by sodium starch glycolate have shown *in vitro* dispersion time of 34 and 26 seconds which was less than other formulations and wetting time was also less (54, 45sec.). Among the formulations the most promising one is F6 containing 10% sodium starch glycolate with 10% camphor showing 93.01% drug release indicating better drug release and improved bioavailability. So it was concluded that sublimation method along with superdisintegrant addition was excellent method in formulation of fast dissolving tablets of Promethazine HCl which gives quick relief from emesis.

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