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Development and Evaluation of Taste-Masked Rapid Dissolving Tablets of Cetrizine hydrochloride

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ABSTRACT

Allergy is common problem among all age groups. Similarly difficulty in swallowing is common especially in elderly and pediatrics. Mouth dissolving tablets constitute an innovative dosage forms that overcome the problems of swallowing and provides a quick onset of action. The purpose of this study was to formulate and evaluate rapid dissolving tablet of cetrizine hydrochloride using camphor and menthol as sublimating agent. Tablets were prepared by sublimation technique. Six different formulations were prepared. The tablets were evaluated for hardness, uniformity of weight, friability, wetting time, disintegration time and in vitro drug release. The best formulation was selected on the basis of least wetting and disintegrating time and better drug release.

Keywords: Cetrizine hydrochloride; sublimation; menthol; camphor; wetting time.

INTRODUCTION

Mouth dissolving tablets are gaining importance as a potential drug delivery system. This dosage form dissolves and disintegrates in the oral cavity within minutes without need of water or chewing. This formulation is useful in administration of drug in pediatric, geriatric patients [1]. Several approaches have been employed to formulate mouth dissolving tablet which include freeze drying, sublimation, spray drying, addition of disintegrants, and use of sugar base excipients [2]. Cetirizine hydrochloride (CTZ) (±)-[2-[4-[(4-chlorophenyl)phenylmethyl]-1-piperazinyl]ethoxy]- acetic acid is an orally active and selective H_1-receptor antagonist used to treat seasonal allergic rhinitis, perennial allergic rhinitis, and chronic urticaria. CTZ is a white, crystalline water-soluble drug with a bitter taste [3]. Cetirizine competes with histamine for

binding at H_1-receptor sites on the effector cell surface, resulting in suppression of histaminic edema, flare, and pruritus. In present study an attempt has been made to prepare taste masked rapid dissolving tablets of drug by sublimation method using camphor and menthol as sublimating agent.

EXPERIMENTAL SECTION

Materials

Cetrizine hydrochloride was obtained as gift sample from Bracure Pharmaceuticals limited Bhiwadi, camphor, menthol, lactose, sodium sachharin and magnesium stearate were purchased from central drug house New Delhi and Talc from S J Chemicals.

Six different formulations (coded F1 – F6) were prepared containing drug and other excipients as shown in table 1. The drug was mixed with the excipients and was compressed in tablets by using CADMACH SMS25 single punch tablet machine at a fixed compression force of 400 kgf. Formulations were kept in oven at 60^0C for 1 hour so that the sublimating agent sublimizes from tablets leaving pores in tablets.

Table 1. Composition of Tablet formulations 100mg (F1- F6)

Ingredients(mg)	F1	F2	F3	F4	F5	F6
Cetrizine HCl	10	10	10	10	10	10
Camphor	10	15	20	-	-	-
Menthol	-	-	-	10	15	20
Saccharin sodium	5	5	5	5	5	5
Talc	5	5	5	5	5	5
Aerosil	3	3	3	3	3	3
Lactose	67	62	57	67	62	57

Evaluation Parameters

Drug content Twenty tablets were weighed and powdered. An amount of the powder equivalent to 10 mg of cetrizine hydrochloride was dissolved in 100ml of pH 6.4 phosphate buffer, filtered, diluted suitably and analyzed for drug content at 232nm using UV-Visible spectrophotometer (UV 160- Shimadzu, Japan).

Weight Variation Twenty tablets were selected at a random and average weight was calculated. Then individual tablets were weighed and the individual weight was compared with an average weight [4].

Hardness The strength of tablet is expressed as tensile strength (kg/cm^2). The tablet crushing load, which is the force required to break a tablet by compression[4]. It was measured using a tablet hardness tester (Pfizer Hardness Tester).

Friability Friability test is performed to assess the effect of friction and shocks, which may often cause tablet to chip, cap or break. Roche friabilator was used for the Purpose. This device subjects number of tablets to the combined effect of abrasion and shock by utilizing a plastic chamber that revolves at 25 rpm dropping the tablets at a distance of 6 inches with each revolution. Preweighed sample of tablets was placed in the friabilator, which was then operated for 100 revolutions. Tablets were dusted and reweighed. Compressed tablets should not loose more than 1% of their weight [5].

Wetting time The wetting time of the tablets was measured using a simple procedure. Five circular tissue papers were placed in a Petri dish which covered the entire surface area of Petri dish. 10 ml of water at 37 ± 0.5 ºC containing eosin, a water-soluble dye, was added to the Petri dish. A tablet was carefully placed on the surface of tissue paper. The time required for water to reach the upper surface of the tablets was noted as the wetting time [6].

Disintegration time Disintegration time was measured using a modified disintegration method. For this purpose, a Petri dish was filled with 10 ml of water at 37 ± 0.5 ºC. The tablet was carefully put in the center of the Petri dish and the time for the tablet to completely disintegrate into fine particles was noted [6].

***In vitro* drug release** The *in vitro* dissolution study was carried out in a USP dissolution test apparatus (TDT-OP Electrolab, Mumbai India), type 2 (paddle) with a dissolution media of 900 mL of 0.1 M hydrochloric acid at 50 rpm (37 ºC ± 0.5 ºC). Samples were withdrawn at the end of 30 min and the dissolution of drug was expressed as % drug dissolved at the end of 30 minute [7].

Statistical analysis All data are expressed as mean ± standard deviation.

RESULT AND DISCUSSION

The results of Drug content, Weight variation, Hardness, Friability, Wetting time, Disintegration time and *in vitro* drug release are shown in table 2 and figure 1.

Table 2. Comparative data of various evaluating parameters of formulations (F1-F6)

Parameters	F1	F2	F3	F4	F5	F6
Drug content (%)	98.34±0.34	98.14±0.25	99.43±0.43	99.10±0.28	98.29±0.12	100.67±0.38
Weight variation	Passes	Passes	Passes	Passes	Passes	Passes
Hardness*	3.6±1.1	3.8±1.5	4.1±1.9	3.2±1.1	3.4±1.4	3.9±1.3
Friability (%)	0.567	0.532	0.765	0.423	0.565	0.658
Wetting time*(sec)	54±1.2	43±1.1	37±11.6	48±1.8	34±1.4	25±1.3
Disintegra-tion time (sec)	45±1.3	37±0.67	29±0.98	40±1.4	30±1.9	20±0.35
***In vitro* drug release at 30 min(%)**	96.03±1.2	97.93±1.3	98.43±0.9	95.10±1.4	98.29±1.1	100.10±0.8

*All values are expressed as mean ± SD, n=3

The percentages drug contents of all the tablets were found to be between 98.14±0.25% to 100.67±0.38% which was within the acceptable limits and indicates that the drug is uniformly distributed in the formulations. All the tablets passed weight variation test as the percentage weight variation was within the pharmacopoeial limits. The weight of all the tablets was found to be uniform with low standard deviation values indicating efficient mixing of drug and excipients.

Hardness of the tablets was found to be 3.4±1.4 to 4.1±1.9 kg/cm² for all the formulations indicating good mechanical strength with an ability to withstand physical and mechanical stress conditions while handling hardness and in acceptable limit for rapid dissolving tablets. Friability below 1% was an indication of good mechanical resistance of the tablets and also meets the IP limits.

Menthol containing tablets exhibited faster disintegration as compared with tablets containing camphor. The porous structure is responsible for faster water uptake; hence it facilitates wicking action in bringing about faster disintegration in the mouth. The results of in-vitro wetting time and in-vitro disintegration time of all the tablets were found to be within the prescribe limits and satisfy the criteria of rapid dissolving tablets. The *in vitro* wetting time was found to be in the range of 25±1.3 to 54±1.2 seconds while the *in vitro* disintegration time was founds in the range of 20±0.35 to 45±1.3 seconds respectively. It was observed that when menthol was used as sublimating agent, the tablets disintegrates rapidly within less time as compared to the tablets containing camphor as sublimating agent. The same results were obtained in case of wetting time. Comparatively increased concentration of camphor (in formulations F2 and F3) and menthol (in formulation F5 and F6) showed relatively decreased wetting time and *in vitro* disintegrating time which may be attributed to faster uptake of water due to the porous structure formed during sublimation of camphor and menthol thus facilitating to bring about faster wetting and disintegration.

The *in vitro* drug release data at 30 minutes of all the formulations are mentioned in the table no.2. The results revealed that the overall cumulative drug release at 30 min was found to be within range of 95.10±1.4 to 100.10±0.8. The drug release from all batches was found to be concentration dependent following first order release kinetics (8), which is indicative of rapid absorption and improved bioavailability. The formulation F6 with least disintegrating time of 20±0.35 seconds and maximum drug release 100.10±0.8 % was selected as best formulation among the all formulations prepared.

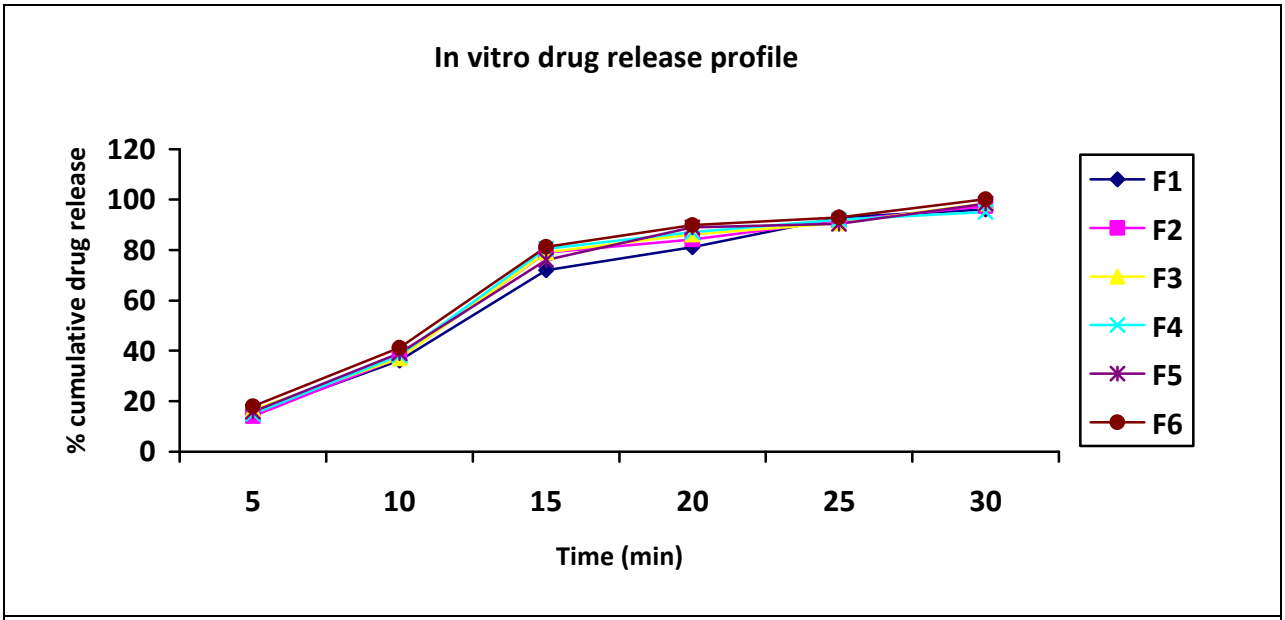

Figure 1. Comparative data of various evaluating parameters of formulations (F1-F6)

CONCLUSION

Overall, the results suggest that suitably formulated mouth-dissolving tablets of cetrizine hydrochloride containing camphor and menthol as a subliming agent can be achieved. The tablets exhibited good i*n vitro* disintegrating time and wetting properties in presence of subliming agent. Thus the present study demonstrated potentials for rapid absorption, improved bioavailability, effective therapy and patient compliance.

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