Preparation and Evaluation of Mouth Dissolving Tablets of Salbutamol Sulphate

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Asthma is an inflammatory disorder that results in the obstruction of air pathways and causes difficulty in breathing. Amongst the currently available means of treatment, oral dosage forms are associated with lag time and delayed onset of action. However, aerosols and parenterals have rapid onset of action but strongly affect patient compliance. Thus, an attempt was made to improve the onset of action of bronchodilator used commonly in the treatment of asthma. Fast dissolving tablets of salbutamol sulphate were prepared using sublimable ingredients. Selection of the filler also had an important role in deciding the disintegration time. Evaluation of the tablets showed that all the tablets were found to be within official limits and the disintegration time for the formulations ranged from 5 s to 40 s. Amongst all, the formulation containing microcrystalline cellulose and ammonium bicarbonate showed the least disintegration time of 5 s.

Asthma is a chronic inflammatory disease, which includes bronchial hyperactivity and bronchospasm[1] characterized by hyper responsiveness of tracheo-brochial smooth muscle to variety of stimuli[1,2], resulting in narrowing of air tubes, often accompanied by increased secretions and mucosal edema resulting in breathlessness or dyspnea, wheezing cough, chest congestion and anxiety about being unable to breathe[1-3].

Asthma affects over 5-10% of population in industrialized countries[4]. It afflicts approximately 53 million people across world mostly in United States,

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France, Germany, Italy, Spain, United Kingdom, and Japan[4,5]. More than 4000 people die every year in India as result of complications arising from serious asthma attacks[4] though there are several recommendations and treatments being reported[4].

The treatment of asthmatic symptoms generally includes conventional oral dosage forms like tablets, capsules, oral liquids etc.; inhalation therapy includes metered dose inhalers with or without spacers, dry powder inhalers, and other aerosol systems[1-3]. Oral administration is the most widely accepted route of delivery due to its ease of administration, convenience, versatility and most importantly patient compliance. Several new technologies for oral delivery have recently been available to address the problems of physicochemical and pharmacokinetic characteristic of drugs, while improving patient compliance. One of these include fast dissolving technology which offers the advantages of both solids and liquids such as quick disintegration and dissolution of tablets, no residue in mouth, requires no water intake, provides a pleasant mouth feel and even allows high drug load.

An attempt was made for preparation of fast dissolving tablets of a model bronchodilator, salbutamol sulphate with an aim of reducing the lag time and providing faster onset of action to relieve immediately acute asthmatic attack. This would be advantageous as conventional solid oral dosage forms are often associated with a longer lag time and thus slower onset of action, while oral liquids prove to have faster onset of action but require careful handling. Aerosol systems are specific but fail to deliver the actual dose of drug with only ten percent of administered dose deposited on the bronchi while rest of the drug is deposited in oropharynx and is swallowed. Also, metered dose system are less potable while dry powder inhalers cause clogging of device and require skillful operation. A fast dissolving tablet form would thus be advantageous, as salbutamol sulphate is water-soluble and its preparation into a fast dissolving form would render it to dissolve rapidly and thereby result in rapid absorption without any lag time[2].

Salbutamol sulphate was obtained as a gift sample from Eros Pharma, Bangalore, microcrystalline cellulose (AR) was purchased from Loba chemie, Mumbai; ammonium bicarbonate (AR) was purchased from Merck Ltd, Mumbai; mannitol from Loba chemie Mumbai while magnesium stearate and talc were purchased from S. D. Fine Chemicals, Mumbai.

Tablets were prepared by wet granulation process using sublimable components viz. camphor and ammonium bicarbonate. Four different tablets having different combination of sublimable excipients were prepared (Table 1). Excipients were screened through sieve 44 and mixed with drug. The above blend was granulated with non-aqueous granulating agent, polyvinyl pyrrolidone (PVP) in alcohol through sieve 44. The granules were air-dried and evaluated for granular properties. The dried granules were the mixed with lubricant magnesium stearate and glidant talc and compressed into tablets. Tablets were subjected for drying at a temperature of 50° to facilitate the volatilization of sublimable components added. The tablets were weighed at regular intervals until constant weight was achieved ensuring complete removal of the sublimable component. The tablets were then subjected to the following evaluations including weight variation, friability, hardness, disintegration test and drug content determination.

Drug content was determined by dissolving one tablet in 100 ml distilled water. An aliquot of 2 ml sample was withdrawn and diluted to 10 ml and analyzed by UV spectrophotometer at 276 nm against blank prepared by using dummy tablets treated in a similar

TABLE 1: COMPOSITION OF MOUTH DISSOLVING TABLETS

Ingredient	Formulation 1 (mg/tablet)	Formulation 2 (mg/tablet)	Formulation 3 (mg/tablet)	Formulation 4 (mg/tablet)
Salbutamol	2	2	2	2
Ammonium bicarbonate	-	-	12.5	12.5
Camphor	12.5	12.5	-	-
Microcrystalline cellulose	-	20	20	-
Mannitol	20	-	-	20
PVP in alcohol	5	5	5	5
Sodium saccharine	0.5	0.5	0.5	0.5
Magnesium stearate	5	5	5	5
Talc	5	5	5	5

TABLE 2: EVALUATION OF FAST DISSOLVING SALBUTAMOL TABLET FORMULATIONS

Parameter*	F_1	F_2	F_3	F_4
Weight variation (mg/ tablet)	49.8±0.523	48±0.610	49.9±0.431	47.3±0.587
Hardness (kg/cm^2)	3.5±0.30	3.8±0.20	3.4±0.11	3.5±0.26
Friability (in %)	0.3±0.11	0.8±0.05	0.4±0.09	0.7±0.10
Disintegration time (sec.)	40±1.21	10±1.21	5±1.15	25±1.0
Drug content (%)	97.5±0.20	96.4±0.31	98.8± 0.14	98.17± 0.08

*Average of three readings, n = 3

manner. The results of all evaluations are shown in Table 2.

Fast dissolving tablets of salbutamol sulphate could be prepared successfully using sublimable ingredients. Drying at 50^o rendered tablets porous by allowing the volatile components to escape through the tablet matrix. The tablets were found to be porous after drying thus facilitating their easier breakup in water.

The formulation containing microcrystalline cellulose as filler showed minimum disintegration time which could be attributed towards disintegrating property of microcrystalline cellulose. However, the formulations containing mannitol as filler showed longer disintegration time, which could be, attributed to slower dissolution characteristics of mannitol. The tablets containing a combination of mannitol and camphor or tablets containing microcrystalline cellulose and camphor showed longer disintegration time while the combination comprising of mannitol and ammonium bi carbonate or microcrystalline cellulose and ammonium bicarbonate showed least disintegration time, indicating that the disintegration properties of tablets were influenced by the presence of the type of volatilizable component and filler used.

However, all the prepared tablets were found to disintegrate fast showing disintegration time of less than a minute. Amongst the prepared formulations, F_3 was found to have the minimum disintegration time of 5 s. Formulations tested for all the official tests for tablets and were found to be within limits. Thus, it can be concluded that fast dissolving can be prepared with a view of obtaining faster action of the drug and would be advantageous in comparison to the currently available conventional forms. The technique adopted was found to be economical and industrially feasible. Salbutamol sulphate being a water-soluble drug would be readily available in a dissolved form for rapid oral uptake. The rapid dissolving concept in case of salbutamol sulphate could be of a great importance in relieving acute asthmatic shocks.

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REFERENCES

1. Gibbs KP, Small M. Asthma and its complications. *In*: Walker R, Edwards C, editors. Clinical pharmacy and therapeutics, 3rd ed. Toronto; Elsevier Science Publisher: 2003. p. 567-94.
2. Bradley JU, Lawrence ML. Drugs used in treatment of asthma. *In*: Hardman JG, Lee E., editors. Goodman and Gillman's: The pharmacological basis of therapeutics, 10th ed. New York; The Mc Graw-Hill Companies: 2001. p. 735.
3. Peter JB, Robert AM, George RB, editors. Principles of pharmacology: Basic concepts and clinical applications. New York; Thomson Publishing Company: 1995. p. 589.
4. Chang RK, Guo X, Burnside B, Couch R. Fast-dissolving tablets. Pharm Technol 2000;24:52-8.
5. Biradar SS, Bhagavati ST, Kuppasad IJ. Fast dissolving drug delivery systems: A brief overview. Int J Pharmacol 2006;4:2.
6. Patil RY, Chate RS, Bande YA. Fast dissolving tablets of metaprolol. Chron Pharmabiz 2002;56.
7. Rozer R, Riegelman S, Yang KY, Cheng KC. Fast dissolving drug delivery systems: Techniques and methods. Eur Respir J 1998;12:315.
8. Reddy LH, Ghosh B, Rajneesh. Fast dissolving drug delivery systems: A review of the literature. Indian J Pharm Sci 2002;64:331-6.
9. Bell H, Cristi D, Thomas F, Hausberger, Angela G. US patent no., US 200202171, 2002.
10. Green R, Patric K. US Patent No., US 20010055611, 2001.

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