RESEARCH ARTICLE

Formulation and characterization of fast-dissolving tablet of promethazine theoclate

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Fast-dissolving tablets (FDT) of promethazine theoclate were prepared by direct-compression method after incorporating superdisintegrants Ac-Di-Sol, Sodium Starch Glycolate (SSG), and Crospovidone in different concentrations. Nine formulations having superdisintegrants at different concentration levels were prepared to assess their efficiency and critical concentration level. Different types of evaluation parameters for tablets were used. Tablets containing Ac- Di- Sol showed superior organoleptic properties, along with excellent *in vitro* and *in vivo* dispersion time and drug release, as compared to other formulations.

Key words: *Direct compression, promethazine theoclate, superdisintegrant*

INTRODUCTION

Promethazine theoclate, dimethyl (1-methyl-2-phenothiazin-10-ylethyl) amine salt of 8-chlorotheophylline, a novel antihistaminic with antimuscarinic and some serotonin-antagonist properties, is indicated for its antiemetic action in the prevention and treatment of nausea and vomiting in conditions such as motion sickness, drug-induced vomiting, and postoperative vomiting.[1] Although it has excellent oral bioavailability (25%), its poor aqueous solubility (10 μg/mL, 25°C) makes its absorption and dissolution rate limited and thus delays onset of action.

Many patients find it difficult to swallow tablets and hard gelatin capsules and thus do not comply with prescription, which results in high incidence of noncompliance and ineffective therapy.[2] Fast-disintegrating tablets are gaining prominence as new drug-delivery systems. These dosage forms dissolve or disintegrate in the oral cavity within a minute without the need of water or chewing.[3]

The objective of this study was to enhance safety and efficacy of drug molecule, achieve better compliance, solve the problem of difficulty in swallowing, enhance onset of action, and provide stable dosage form.

EXPERIMENTAL

Promethazine theoclate (PMT) was received as a gift sample from Mehta Chemicals (Mumbai, India). Ac-Di-Sol, Crospovidone, sodium starch glycolate, and Avicel were gifted by Signet Chemicals (Mumbai). All reagents and solvents used were of analytical grade.

Preparation of blends and tablets

The superdisintegrants (Ac-Di-Sol, Crospovidone, sodium starch glycolate) in varying concentration (02-04%) were used to develop the tablets. All the ingredients (shown in Table 1) were passed through mesh no. 60. All the ingredients were co-ground in a pestle motor for 5 minutes. The mixed blend of excipients was compressed using a single-punch machine to produce convex-faced tablets weighing 100 mg each, with thickness of 2.85 mm and diameter of 9 mm. A minimum of 50 tablets were prepared for every batch.[4]

Evaluation of blends

The quality of tablet, once formulated by rule, is generally dictated by the quality of physicochemical properties of blends. There are many formulation variables and process variables involved in the mixing step, and all these can affect the characteristics of blends produced. The blends were characterized by mass-volume relationship (bulk density, tapped density, Hausner's ratio, compressibility index) and flow properties (static angle of repose).[5]

Evaluation of tablets

Prepared tablets were evaluated for hardness (Monsanto hardness tester), friability (Roche friabilator), weight variation, *in vitro* dispersion time, and drug content.[6,7] *In vitro* dissolution studies of fast-dissolving tablets were performed by using type II apparatus as specified

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in United State Pharmacopoeia at 100 rpm; and Sorenson's buffer (pH, 6.8), 900 mL, was used as dissolution medium. Temperature of dissolution medium was maintained at 37°C ± 0.5°C. Aliquot of dissolution medium was withdrawn at a specific time interval and it was filtered. Absorption of filtered solution was checked by UV spectroscopy (Shimadzu, Japan), and drug content was determined from standard calibration curve. Dissolution rate was studied for all designed formulations and conventional tablet.[8]

RESULT AND DISCUSSION

The use of superdisintegrants for preparation of fast-dissolving tablets is highly effective and commercially feasible. These superdisintegrants accelerate disintegration of tablets by virtue of their ability to absorb a large amount of water when exposed to an aqueous environment. The absorption of water results in breaking of tablets and therefore faster disintegration. This disintegration is reported to have an effect on dissolution characteristics as well.

Prepared fast-dissolving tablet gets dispersed in the mouth quickly and releases the drug early as compared to its formulated conventional tablet. Three different superdisintegrants - Ac-D-Sol, Crospovidone, and sodium starch glycolate - were tried to achieve fast dispersion of tablets. Blends evaluated [Table 2] were found to have excellent flowability as determined by angle of repose and compressibility-flowability correlation data. However, tablets containing Ac-Di-Sol showed the fastest disintegration, as shown in Figure 1. Characteristics of tablets are tabulated in Table 2. *In vitro* dissolution studies [Figure 2] for F3 confirmed the results. F3 tablet showed good dissolution efficiency and rapid dissolution. The study shows that the dissolution rate of promethazine theoclate can be enhanced to a great extent by direct-compression

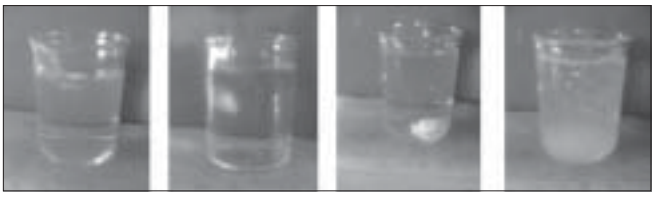

Figure 1: *In vitro* disintegration of formulation F3

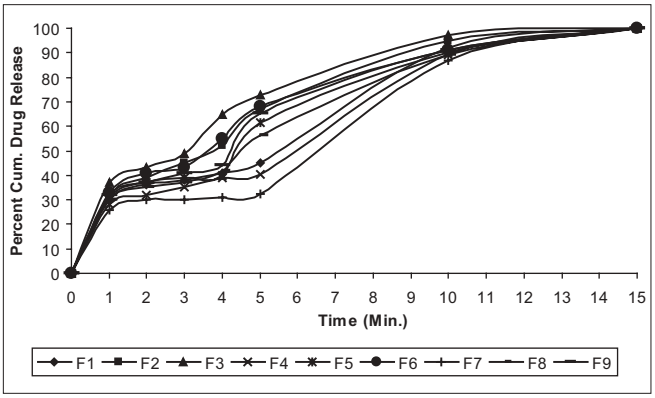

Figure 2: *In vitro* dissolution profile of prepared formulations

Table 1: Formulation of fast-dissolving tablet of promethazine theoclate

Formulation ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Promethazine theoclate	25	25	25	25	25	25	25	25	25
Ac- Di- Sol	2	3	4	-	-	-	-	-	-
Crospovidone	-	-	-	2	3	4	-	-	-
Sodium starch glycolate	-	-	-	-	-	-	2	3	4
Avicel Ph 102	20	20	20	20	20	20	20	20	20
Lactose	25	25	25	25	25	25	25	25	25
Mannitol	25	24	23	25	24	23	25	24	23
Mg. Stereate	1	1	1	1	1	1	1	1	1
Talc	2	2	2	2	2	2	2	2	2

Table 2: Evaluation of fast-dissolving tablet of promethazine theoclate

Formulation parameters	F1	F2	F3	F4	F5	F6	F7	F8	F9
Bulk density (gm/cm^3)	0.418	0.424	0.431	0.421	0.398	0.403	0.416	0.422	0.428
Tapped density (gm/cm^3)	0.469	0.473	0.475	0.465	0.439	0.441	0.468	0.461	0.472
Hausners ratio	1.122	1.115	1.102	1.104	1.103	1.094	1.125	1.092	1.102
Compressibilty Index (%)	10.874	10.359	9.263	9.462	9.339	8.616	11.111	8.459	9.322
Angle of repose (°)	25.35	24.89	23.44	26.34	25.42	26.13	24.19	25.27	24.54
Weight (mg)	101.24	100.46	100.54	101.19	101.08	100.36	100.03	100.59	101.25
Hardness (kg/cm^2)	2.5	2.4	2.4	2.7	2.6	2.4	2.6	2.6	2.5
Friability (%)	0.87	0.92	0.093	0.078	0.082	0.091	0.088	0.86	0.71
Disintegration time (sec)	78.51	66.38	52.17	79.06	68.15	55.28	83.05	75.34	67.81
Swelling time (sec)	65.23	51.38	49.02	68.29	55.56	51.21	72.59	68.33	61.27
% Drug release (5 min)	45.093	67.139	72.571	40.531	61.719	68.091	32.498	56.496	65.369

technique with the addition of superdisintegrants, which gives quick relief from emesis.

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Source of Support: Nil, **Conflict of Interest:** None declared.