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FORMULATION DEVELOPMENT AND EVALUATION OF DAPSONE ORAL MOUTH DISSOLVING TABLETS

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ABSTRACT

The purpose of this research was to develop mouth dissolve tablets of dapsone using sodium starch glycolate (SSG), crospovidone (CP), croscarmellose sodium (CCS) and other directly compressible excipients by direct compression method. The designed oral mouth dissolving of dapsone will be evaluated for hardness, friability, and weight variation, *in vitro* dispersion time, wetting time, water absorption ratio, drug content uniformity and *in vitro* dissolution rate. *In vitro* drug release study was carried out in 0.1N HCL (PH 1.2) and based on the results, F-6 was identified as the best formulation among all the other formulations and *in vitro* release profiles was 99% of drug release within 30 minutes. Dapsone is described as being active against *Mycobacterium leprae*, hence its role in the treatment of leprosy and related pathologies.

INTRODUCTION:

Due to ease of administration, patient compliance and acceptability the oral route is most widely accepted route[1]. Difficulty swallowing is particularly experienced by pediatric and geriatric patients[2]. Accordingly, a new delivery system known as fast dissolving gaining importance[3]. Without water patient can be swallowed easily and dissolve rapidly in saliva[4]. Bitterness elimination is a main condition in product formulation of mouth dissolving tablets[5]. They offer an advantage over swallowing tablets and capsules[6]. A technique that is frequently employed in the preparation of mouth dissolving tablets include, freeze drying, sublimation, spray drying, molding, mass extrusion and direct compression[7-10]. For better dissolution and bioavailability of drug add superdisintegrants in the formulation[11, 12]. Dapsone is a sulphone and is active against a wide variety of bacteria[13]. The mechanism of action is probably similar to sulfonamides, which involves inhibition of folic acid synthesis in susceptible organisms[14].

MATERIALS:

Dapsone was obtained from Pharma Train, microcrystalline cellulose (MCC), (Avicel PH 102), Ac-Di-Sol (CCS), polyplasdonexl (CP), explotab (SSG), lactose, mannitol From Sd. Fine Chemicals, Mumbai, India.

METHODOLOGY

Pre Compression Studies: The powder mixtures of different formulations were evaluated for angle of repose, bulk density (apparent and tapped) and compressibility index[15].

Direct compression method: All the ingredients were powdered separately and passed through # 40 mesh sieve separately. The drug and directly compressible excipient were mixed by adding small portion of each at a time and blending it to get a uniform mixture and kept aside. Then the other ingredients were mixed in geometrical order, in an inflated polyethylene pouch magnesium stearate and talc were added last and mixed for a further two minutes and the tablets were compressed using 6 mm flat round punches to get tablets of 150 mg weight[16].

Post Compression Studies: The prepared tablets were studied for their physical properties like weight variation, hardness, friability and drug content uniformity[17]

RESULT AND DISCUSSION:

Initially, by using UV-Visible spectrophotometer the pure dapsone was scanned under UV-range between 200-400 nm for absorption spectrum. In the range between 2-10 µg/ml concentrations of dapsone was prepared by using 0.1N HCl as a medium and the maximum absorbance (λ_{max}) for dapsone was found at 257 nm. Dapsone showed good linearity between 2-10 µg/ml with a correlation coefficient of 0.999. The drug excipients compatibility study was carried out by using FTIR (shown in Fig 1 and Fig 2). From the results it was concluded that the drug was compatible with superdisintegrants and other excipients used in the formulation. Dapsone tablets were prepared successfully by using different superdisintigranting agents like SSG, CP and CCS by direct compression method (Table 1). The powder mixtures of different formulations were evaluated for angle of repose, bulk density (apparent and tapped) and compressibility index. The results of angle of repose (<40) and Carr's index (<22) indicated fair to passable flow properties of the powder mixture and their values are shown in Table 2. After pre-compression evaluation, blend was compressed into tablet form using 7.0 mm punch. After preparation of tablets, various physicochemical properties were studied such as diameter, weight variation, hardness, thickness, friability and drug content. The physical properties are shown in Table 3 and based on the results; all the formulations were obtained within pharmacopoeial limits The USP dissolution apparatus –II (Lab India, India) was used for all the *in vitro* dissolution studies. In this method, the tablet was placed inside the dissolution vessel containing 500ml of 0.1N HCl medium. 5 ml of sample was withdrawn at time intervals of 5 min. up to 30min. The volume of dissolution fluid was adjusted to 500 ml by replacing fresh 5ml of dissolution medium after each sampling. The mouth disintegrating tablets of dapsone developed in this investigation releases drug within 30 minutes. Thus, we are able to achieve our objective of preparing mouth disintegrating tablets of Dapsone with minimum super disintegrants and simple method of manufacture. The drug content of the tablets was found between 99.12±0.55 mg to 100.87±0.68 mg of Dapsone. Formulation F1 and F6 showed fast (Show in Fig 3 and Fig 4) disintegration compared to formulation F7 to F10 (Shown in Fig 5). When compare to all prepared formulations, F6 shows good physicochemical characteristics and better drug release. All superdisintegrants have high water absorption capacity and cause swelling.

Table 1: Composition of mouth disintegrating tablets of dapsone (mg/tablet)

Ingredients	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**	**F10**
Dapsone	10	10	10	10	10	10	10	10	10	10
SSG	20	40	60	-	-	-	-	-	-	-
CP	-	-	-	20	40	60	-	-	-	60
CCS	-	-	-	-	-	-	20	40	60	-
Mannitol	60	60	60	60	60	60	60	60	60	60
Lactose	-	-	-	-	-	-	-	-	-	12
MCC pH 102	52	32	12	52	32	12	52	32	12	-
Aspartame	5	5	5	5	5	5	5	5	5	5
Peppermint oil	1	1	1	1	1	1	1	1	1	1
Talc	1	1	1	1	1	1	1	1	1	1
Magnesium stearate	1	1	1	1	1	1	1	1	1	1

Table 2: Pre compression studies of prepared Dapsone oral disintegrating tablets

Formulation code	**Bulk density (Kg/cm^3)**	**Tapped density(Kg/cm^3)**	**Cars index (g/cc)**	**Hausner's ratio**	**Angle of repose (°)**
F1	0.40	0.48	16	1.2	32.73
F2	0.39	0.48	18	1.23	34.96
F3	0.50	0.58	13	1.16	28.58
F4	0.44	0.50	12	1.1	27.92
F5	0.37	0.41	9.75	1.1	25.35
F6	0.37	0.41	9.75	1.1	33.14
F7	0.36	0.39	7.6	1.0	27.03
F8	0.41	0.45	8.8	1.0	31.85
F9	0.39	0.48	18	1.23	28.96
F10	0.41	0.45	8.8	1.0	27.85

Table 3: Post compression studies of prepared Dapsone disintegrating tablets

Batch	**Hardness**	**Friability (%)**	**Drug Content (%)**	**Thickness (mm)**	**DT sec**	**WT (sec)**	***In vitro* DT**	**Weight variation**	**Water AB ratio (%)**
F1	3.1	0.45	99.12	2.5	30	45	29	Pass	61.3
F2	2.9	0.62	100.73	2.8	25	42	34	Pass	69.8
F3	3.3	0.71	99.74	2.6	20	35	25	Pass	73.4
F4	2.5	0.32	98.98	2.5	31	31	32	Pass	86.2
F5	2.8	0.51	99.67	2.6	27	36	31	Pass	84.12
F6	2.8	0.52	99.83	2.8	25	43	33	Pass	93.4
F7	2.9	0.38	101.32	2.8	31	41	36	Pass	64.3
F8	3.2	0.48	100.87	2.5	26	36	33	Pass	74.8
F9	3.5	0.63	99.74	2.7	24	48	39	Pass	76.1
F10	3.0	0.54	99.86	2.6	32	39	28	Pass	82.3

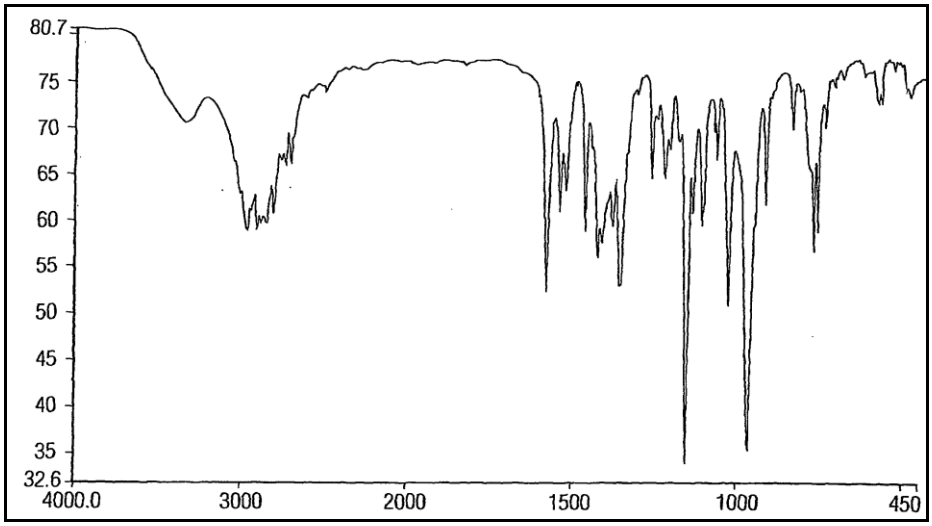


Fig 1: FTIR spectra of pure dapsone

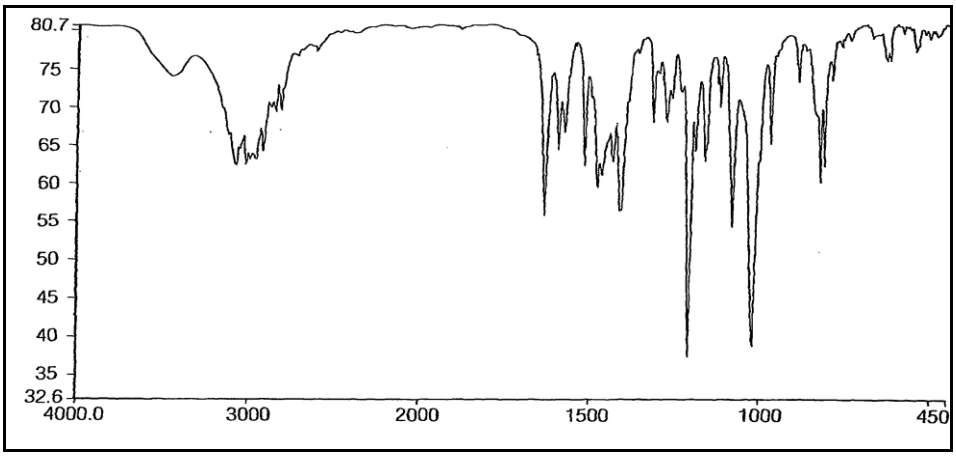


Fig 2: FTIR spectra of optimized formulation (F6)

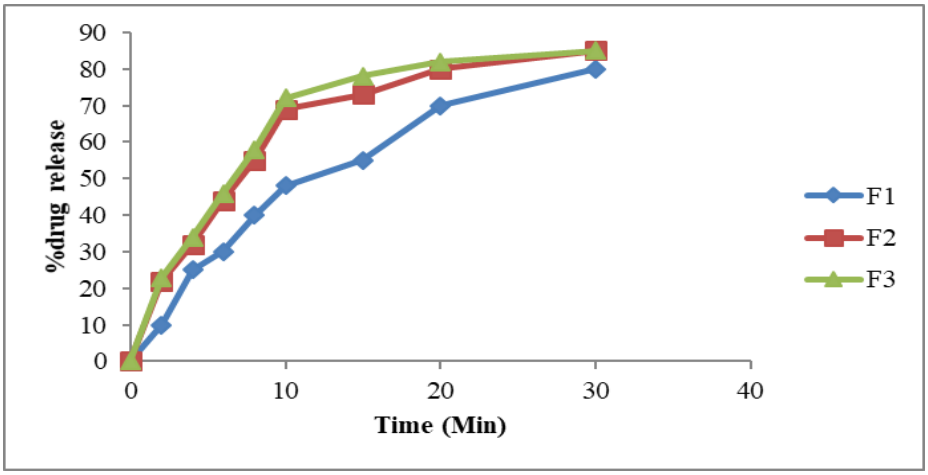


Fig 3: Percentage drug releases of Dapsone containing SSG

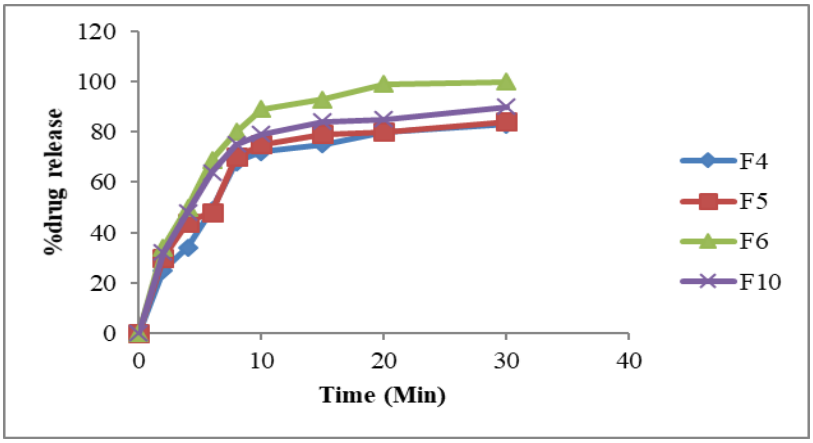
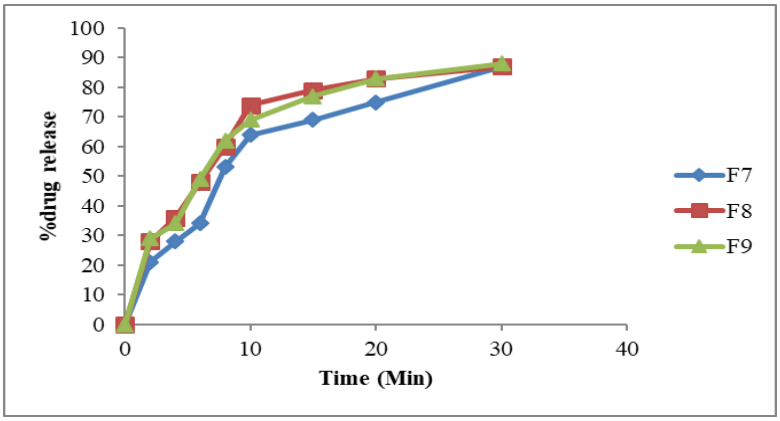


Fig 4: Percentage drug releases of Dapsone containing CCS &

Fig 5 Percentage drug releases of Dapsone containing CP



In vitro dispersion time was measured by the time taken to undergo uniform dispersion. Rapid dispersion within seconds has been observed in all the formulations. This *in vitro* dispersion time gives direct information about super disintegration nature of disintegrants used. All formulations showed disintegration time less than 30 seconds.

CONCLUSION:

From the above study, it was concluded that, by employing commonly available pharmaceutical excipients such as superdisintegrants, hydrophilic and swellable excipients and proper filler, a fast disintegrating tablet of dapsone FDT used in leprosy disorders, were formulated successfully with desired characteristics in combined pharmaceutical dosage form which disintegrated rapidly, providing rapid onset of action and enhancing the patient convenience and compliance.

The technique adopted was found to be economical and industrially feasible. *In vitro* drug release study was carried out and based on the results; F-6 was identified as the best formulation among all the other formulations and i*n vitro* release profiles was 99% within 30 minutes.

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