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RESEARCH ARTICLE

Formulation and Evaluation of Oral mouth dissolving Tablets of Dapsone

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ABSTRACT
The aim of the present study is to formulate the Oral Mouth Dissolving tablets (ODT) of Dapsone using SSg, Crospovidone, Croscarmellose sodium and other directly compressible excepients by direct compression method. Dapsone is a sulfone with anti-inflammatory immunosuppressive properties as well as antibacterial and antibiotic properties. Ten formulations of oral mouth dissolving tablets were prepared using direct compression method with various polymers for different ratios. The evaluation results revealed that all formulations comply with the specification of official pharmacopoeias and/or standard reference with respect to general appearance, content uniformity, hardness, friability and buoyancy. The mouth disintegating 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 excipients and simple method of manufacture.
Key words: Dapsone, Oral mouth dissolving tablets, Direct compression method, Crospovidine, Croscarmellose sodium

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CONTENTS

1. Introduction

An ideal dosage regimen in the drug therapy of any disease is the one, which immediately attains the desire therapeutics concentration of drug in plasma (or at the site of action) and maintains it constant for the entire duration of treatment. This is possible through administration of conventional dosage form in a particular dose and at a particular

frequency. Thus drug may be administered by variety of routes in a variety of dosage forms.

Mouth dissolving tablet:

This is an innovative tablet technology where the dosage form containing active pharmaceutical ingredients disintegrates rapidly, usually in a matter of seconds, without the need for water, providing optimal convenience to the patient. Innovators and inventor companies have given these tablets various names such as orally disintegrating tablets (ODT), mouth dissolving (MD), fast melting, fast dissolving or Orodisperse.

Characteristics of Mouth Dissolving Tablets:

- Convenient and easy to administer as does not require water for oral administration
- Durable and sufficient strength to withstand the rigors of the manufacturing process and manufacturing handling
- Pleasant mouth feel
- Insensitive to environmental conditions such as humidity and temperature.
- Improved taste without any residue in the mouth after disintegration
- Adaptable and amenable to existing processing and packaging machinery
- Cost effective
- Compatible with taste masking

Benefits of Mouth Dissolving Tablets:

- Administered without water, anywhere, any time.
- Suitability for geriatric and pediatric patients, who experience difficulties in swallowing and for the other groups that may experience problems using conventional oral dosage form, due to being mentally ill, the developmentally disable and the patients who are un-cooperative, or are on reduced liquid intake plans or are nauseated.
- Beneficial in cases such as motion sickness, sudden episodes of allergic attack or coughing, where an ultra-rapidonset of action required.
- An increased bioavailability, particularly in cases of insoluble and hydrophobic drugs, due to rapid disintegration and dissolution of these tablets.

2. Materials and Methods

Analytical Method Development

Construction of calibration curve of Dapsone in 0.1N HCL: Working standard: 100mg of Dapsone was weighed and dissolved in 10ml methanol and then make up to a volume of 100ml with 0.1N HCL it give 1000µg/ml concentrated stock solution.

Dilution 1:

From the working standard solution 10ml was diluted to 100ml with 0.1N HCL it will give 100µg/ml concentrated solution. From dilution 1, take 0.2, 0.4, 0.6, 0.8 and 1ml of solution and was diluted up to mark in 10ml volumetric flask to obtain 2, 4, 6, 8 and 10 µg/ml concentrated solutions. This solutions absorbance was noted at λ_{max}=257nm.

Preparation of Oral Disintegrating Tablets

Direct compression method:

Mouth disintegrating tablets of Dapsone were prepared by 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 keptaside. Then the other ingredients were mixed in geometrical order, in an inflated polyethylene pouch magnesium stearate and talc were added last and mixed for further two minutes and the tablets were compressed using 6 mm flat round punches to get tablets of 100 mg weight.

Table 1: List of Ingredients and Manufactures

S.No.	Ingredients	Supplier
1.	Dapsone	Supplied By Pharma Train
2.	Sodium Starch Glycolate	Sd Fine Chemicals, Mumbai
3.	Crospovidone	Nihal Pharma,Hyd
4.	Croscarmellose Sodium	Sd Fine Chemicals, Mumbai
5.	Mannitol	Sd Fine Chemicals,Mumbai
6.	Lactose	Sd Fine Chemicals,Mumbai
7.	Avicel PH102	Sd Fine Chemicals,Mumbai
8.	Aspartame	Sd Fine Chemicals,Mumbai
9.	Peppermint Flavour	Nihal Pharma,Hyd
10	Magnesium Sterate	Sd Fine Chemicals,Mumbai
11	Talc	Sd Fine Chemicals,Mumbai

Table 2: List of Equipment and Companies

S.No.	Name of The Equipment	Model
1	Electronic Weighing Balance	Scale-Tec
2	Friabilator	Roche Friabilator, Electrolab, Mumbai.
3	Compression Machine	Cmd(Cadmach)
4	Tablet Hardness Tester	Pfizer Hardness Tester, Mumbai
5	UV	Lab indiaUV 3000+
6	Dissolution Apparatus	Electro lab TDT-08L
7	Verniercallipers	CD-6"CS

Evaluation of Tablets

The formulated tablets were evaluated for the following Pre, post compression quality control studies and dissolution studies.

In vitro Dissolution Study: 900 ml of 0.1N HCL was placed in the vessel and the USP-II apparatus (Paddle method) was assembled. The medium was allowed to equilibrate to temperature of 37^0C±0.5^0C. A tablet was placed in the vessel and was covered; the apparatus was operated up to 30mins at 50 rpm. At definite time intervals, 5 ml of dissolution medium was withdrawn; filtered and again replaced with 5 ml of fresh medium to maintain sink conditions. Suitable dilutions were done with dissolution medium and were analyzed spectrophotometrically at λ_{max} =257 nm using a UV-spectrophotometer (Lab India).

Release Kinetics: The analysis of drug release mechanism from a pharmaceutical dosage form is an important but complicated process and it is practically evident in case of matrix system. As a model dependent approach the dissolution data are fitted to three popular release models such as zero order, first order, diffusion equations which have been described in the literature. The order of drug release from matrix system was described by zero order kinetics or first order kinetics. The mechanism of drug release from matrix system was studied by Higuchi equation.

Fourier Transform – Spectroscopy:

FT-IR spectra were recorded on samples prepared in potassium bromide disks using thermon electron FTIR. Samples were prepared in potassium bromide discs by means of a hydrostatic press. The scanning range was 400 to 4000 cm^{-1} and the resolution was 4 cm^{-1}. IR spectroscopy has been to quantify the interaction between drug and carrier FTIR spectra of pure drug and best formulation.

3. Results and Discussion

Construction of Standard Calibration Curve of Dapsone in 0.1 N HCl:

The absorbance of the solution was measured at 257nm, using UV spectrometer with 0.1N HCL as blank. The values are shown in table. A graph of absorbance Vs Concentration was plotted which indicated in compliance to Beer's law in the concentration range 2 to 10 µg/ml.

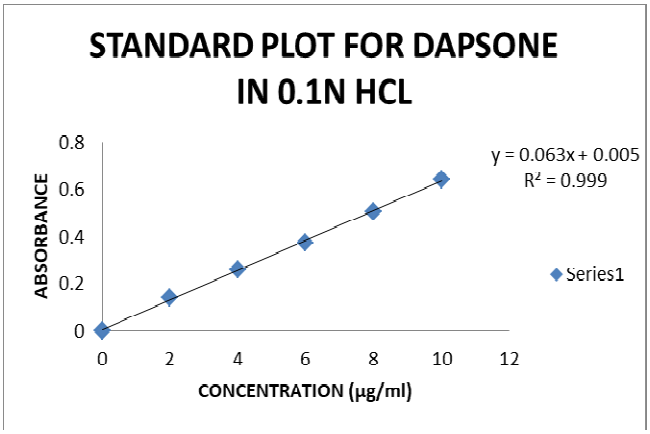


Fig 1: Standard Calibration Curve of Dapsone in 0.1 N HCl

Release kinetics:

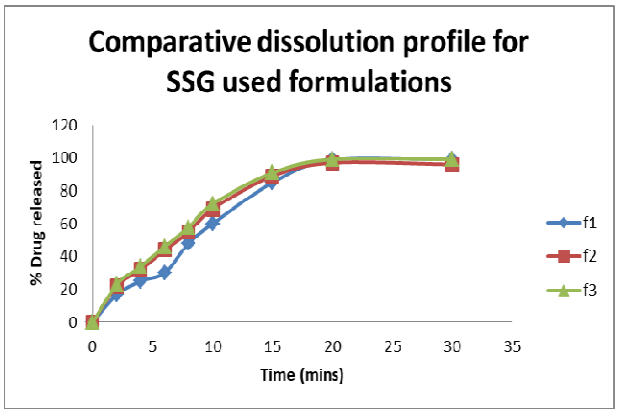


Fig 2: Comparative dissolution profiles for SSG used Formulations

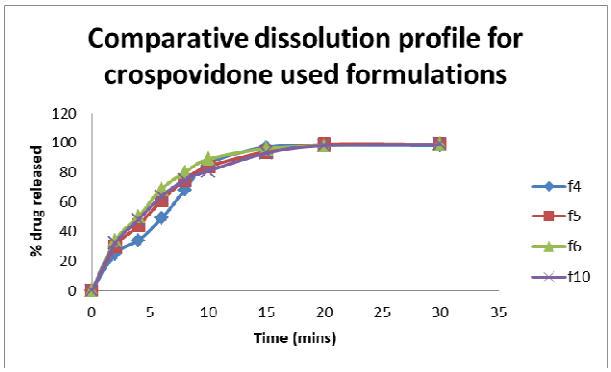


Fig 3: Comparative dissolution profiles for Crospovidone used Formulations

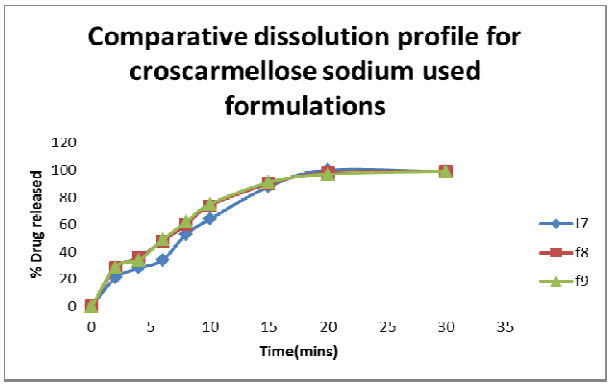


Fig 4: Comparative dissolution profiles for Croscarmellose sodium used Formulations

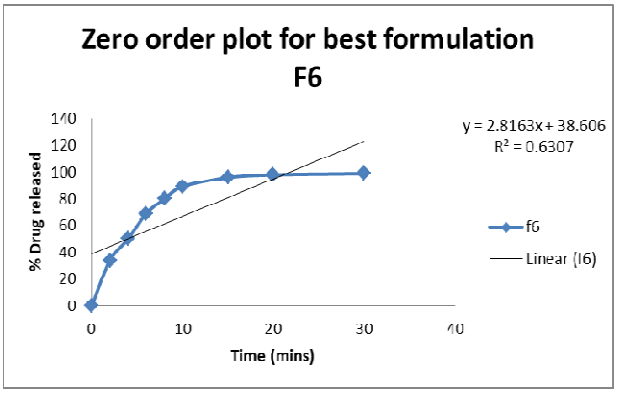


Fig 5: Zero order plot for best formulation F6

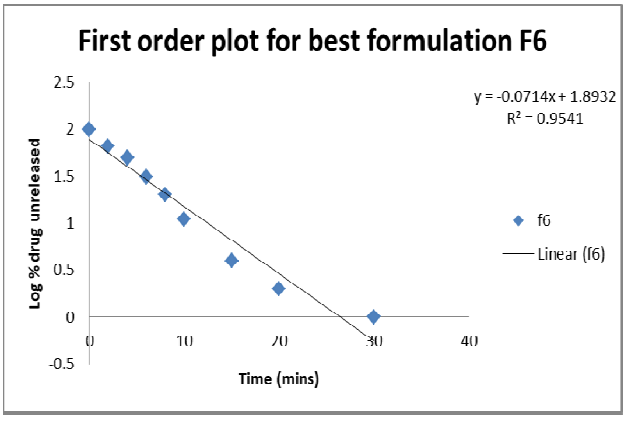
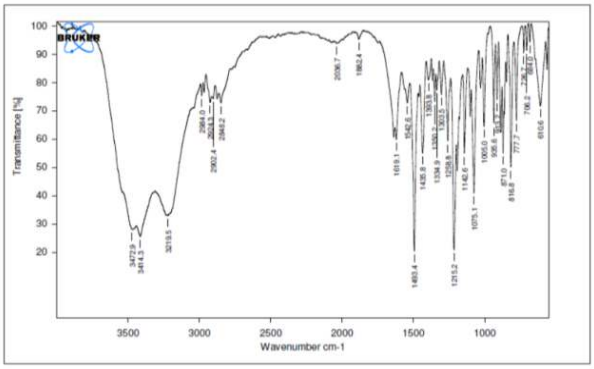


Fig 6: First order plot for best formulation F6

Fig 7: FTIR graph for Dapsone

Fourier Transform – Spectroscopy:



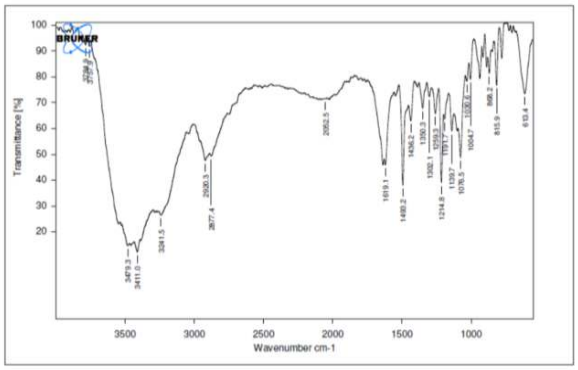


Fig 8:FTIR graph for Dapsone best formulation

Table 3: Formulation of Mouth Disintegrating Tablets of Dapsone

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							
Crospovidone				20	40	60				60
CCS							20	40	60	
Mannitol	60	60	60	60	60	60	60	60	60	60
Lactose	-	-	-	-	-	-	-	-	-	67
MCC pH 102	71	69	67	71	69	67	71	69	67	-
Aspartame	5	5	5	5	5	5	5	5	5	5
Pipperment flavour	1	1	1	1	1	1	1	1	1	1
Talc	1	1	1	1	1	1	1	1	1	1
Megnesium stearate	1	1	1	1	1	1	1	1	1	1
Total weight (mg)	169	187	205	169	187	205	169	187	205	205

Table 4: Standard Calibration Graph Values of Dapsone in 0.1 N HCl

Concentration (µg/ml)	Absorbance
0	0
2	0.141
4	0.26
6	0.372
8	0.507
10	0.64

Table 5: Pre Compression Studies of Dapsone Oral Disintegrating Tablets

Formulation code	Bulk density (Kg/cm^3)	Tapped density (Kg/cm^3)	Cars index	Hausners 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 6: Post Compression Studies for Oral Disintegrating Tablets of Dapsone

Batch	Hardness (kg/cm2)	Friability (%)	Drug Content	Thickness	Disintegration Time	Wetting Time	In vitro dispersio	Weight variation	Water absorption

			(%)	(mm)	(sec)	(sec)	n time		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

Table 7: Dissolution Data of Oral Disintegrating Tablets of Dapsone

Time points (mins)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
0	0	0	0	0	0	0	0	0	0	0
2	17	22	23	25	30	34	21	28	29	32
4	25	32	34	34	44	50	28	36	34	48
6	30	44	46	49	61	69	34	48	49	64
8	48	55	58	68	75	80	53	60	62	75
10	60	69	72	86	84	89	64	74	75	81
15	85	89	91	97	94	96	88	90	91	93
20	99	97	99	98	99	98	100	98	97	98
30	99	96	99	98	99	99	99	99	99	99

4. Conclusion

In the present study, mouth disintegrating tablets were prepared by direct compression method. Mouth disintegrating tablets of Dapsone were successfully prepared using SSG, Crospovidone and Croscarmellose sodium. Evaluation parameters like hardness, friability, weight variation and drug content indicate that values were within permissible limit for all formulations. FTIR spectroscopic studies were carried out in order to establish compatibility between drug and excipients. The result were concluded that there were no chemical intraction between drug and the excipients used. *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 *In vitro* release profiles was 99% within 30 minutes. The Crospovidone used formulation has shown better release profile than compared with other formulations. 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 excipients and simple method of manufacture.

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