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Original Article

Formulation and Evaluation of Taste Masked Orodispersible Tablet of Naproxen Sodium

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ABSTRACT

Objective: The aim of present work is mask the bitter taste of Naproxen sodium and formulate orodispersible tablets of Naproxen sodium.
Experimental work: The bitter taste of drug was masked by using Ion exchange resin orodispersible tablet of Naproxen sodium was prepared by using super disintegrant. All the prepared tablets were evaluated for their pre compression as well as post compression properties.
Results and Discussion: Optimization of Naproxen sodium orodispersible tablet by 3^2 full factorial designs. The independent and dependent factors were concentration of cross providone, concentration of sodium starch glycolate and disintegration time, Drug release (%) respectively. No interaction was found between drug and excipient as confirmed by DSC studies. Optimized formulation shows better post compression property and In-*vitro* drug release.
Conclusions: Orodispersible tablet gives onset of action and quick relief to patient compliance. Oral delivery appears better and effective drug deliverysystem as compared to other drug delivery system. Many ingredients used in the formulation are highly stable and safe for the oral delivery and that pharmaceutical ingredient into ODT is used in treatment of various diseases like joints pain, headaches backaches and Rheumatoid arthritis.

Keywords: Naproxen sodium, Ion exchange resin, Cross povidone, Sodium starch glycolate,

1. INTRODUCTION

Oral route is the most simple and commonly employed route of drug delivery due to its important advantages. It is easy to administer, dosage distribution can be achieved, safest, easy to medicate possible, convenient and economical route. Orally Disintegrating Tablets (ODT) as "A solid dosage form containing medicinal substances, which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue use of various superdisintegrant like crosscarmellose sodium, Sodium starch glycolate and

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Crossprovidone. Naproxen Sodium belongs to the category of analgesic, non-steroidal, non-narcotic, anti-inflammatory agents. Non-steroidal mechanism of action of Naproxen sodium is associated with inhibition of cyclooygenase activity.Naproxen Sodium is used for the treatment of rheumatoid arthritis, osteoarthritis, ankylosing, spondylitis, tendinitis, bursitis and acute gout. The elimination half-life is approximately 15 hours. The ion exchange resin used is Indion 234.It is an effective tablet disintegrant which provides the necessary hardness and chemical stability to the tablet. Depending on the formulation, the use of 0.5% to 5% of Indion 234 is recommended for effective disintegration of the tablet[1-9]

2. MATERIALS AND METHODS

Naproxen Sodium was obtained as a gift sample from Intas pharmaceutics Pvt. Ltd Ahmedabad. Indion resin 234 was obtained from Ion exchange India Ltd, Kolkata. All other excipients were used of analytical grade.

Preparation of complex

Three batches were prepared containing Naproxen Sodium and Indion-234 in the ratio of 1:0.5, 1:1, and 1:1.5. The pH of solution was maintained at pH 7.0. The slurry was stirred for 5 hours. The obtained resinates were separated by filtration, washed with copious quantity of deionized water and drug contents was determined.[10]

Evaluation of complex

Differential Scanning Calorimetery (DSC)

Checking the incompatibilities between Naproxen sodium and ion exchange resin forms an important part of the pre formulation stage during the development of solid dosage form. Differential Scanning Calorimeter (DSC TA-60WS) allows the fast evaluation of incompatibilities, as it is able to show changes in the appearance, shift of melting endotherms and exotherms, and/or variations in the corresponding enthalpies of reaction. The DSC thermograms of pure drug and resinate were recorded. The thermal analysis was performed in a nitrogen atmosphere at a heating rate of 10^0 C/min over a temperature range of 25^0 C to 150^0 C.

Determination of threshold bitterness concentration

Various concentrations (1-30 µg/ml) of drug were prepared in phosphate buffer pH 6.8. Mouth was rinsed with buffer solution and then, l0 ml of most dilute solution was tasted by swirling it in the mouth mainly near the base of the tongue for 30 seconds. If the bitter sensation was no longer felt in the mouth after 30 seconds, the solution was spat out and waited for 1 minute to ascertain whether this is due to delayed sensitivity. Then mouth was rinsed with safe drinking water. The next highest concentration should not be tasted until at least 10 minutes had passed. The threshold bitter concentration is the lowest concentration at which a material continues to provoke a bitter sensation after 30 seconds. After the first series of tests, mouth was rinsed thoroughly with safe drinking water until no bitter sensation remained. Interval of at least 10 minutes was observed between two tests [11-12].

Formulation of orodispersible tablets:

Taste masking of naproxen sodium tablet was done by using Indion-234. Orodispersible tablets of naproxen sodium were prepared by direct compression. All the ingredients were passed through 120-mesh size sieve separately. Then the ingredients were weighed and mixed in geometrical order and compressed into tablet of 380 mg using multi rotary tablet compression machine.

Table 1: Formulation composition of orodispersible tablets

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F8
DRC	172.8	172.8	172.8	172.8	172.8	172.8	172.8	172.8	172.8
SSG	9	12	15	9	12	15	9	12	15
Cross povidone	9	9	9	12	12	12	15	15	15
MCC	127.4	124.4	124.4	124.4	121.4	118.4	121.4	118.4	118.4
Mannitol	50	50	50	50	50	50	50	50	50
Aerosil	4	4	4	4	4	4	4	4	4
Aspartame	4	4	4	4	4	4	4	4	4
Magnesium stearate	3.8	3.8	3.8	3.8	3.8	3.8	3.8	3.8	3.8
Total (mg)	380	380	380	380	380	380	380	380	380

DRC= Drug resin complex**; SSG=** Sodium starch glycolate; **MCC=** Micro crystalline cellulose

Evaluation of orodispersible tablets [13-20]

Weight variation

Twenty tablets were taken at random from each formulation and average weight was determined. Then individual tablets were weighed and the individual weight was compared with the average weight.

Hardness

Three tablets were taken at random from each formulation and hardness was checked using Monsanto Hardness Tester.

Friability

Pre-weighed sample of tablets was placed in the Roche Friabilator tester, which was then operated for 100 revolutions. Tablets were dedusted and reweighed. % Friability was calculated by using the formula

% Friability = $(W_O\text{-}W_f/ W_O) \times 100$

Where W_O = initial weight W_f = final weight

Wetting Time

A piece of tissue paper (12cm x10.75cm) folded twice was placed in a petri dish (10 cm diameter) containing 10 ml of water containing Eosin, a water soluble dye, was added to petri dish. A tablet was carefully placed on the surface of the tissue paper and allowed to wet completely. The time required for water to reach upper surface of the tablet was noted as a wetting time.

% Drug Content

Ten tablets were weighed and crushed in a small glass mortar with pestle. The fine powder was weighed to get 250 mg equivalent resinate of Naproxen sodium and transferred

to 250 ml conical flask containing 100 ml of 0.1N HCl and stirred for 4 hours on magnetic stirrer. Dispersion was filtered and the filtrates obtained were analyzed spectrophotometrically at 273 nm and drug content was determined.

Disintegration Time

The disintegration time was measured using a modified disintegration method (n=6). For this purpose, a petri dish 10cm (in diameter) was filled with 10ml of water. The tablet was carefully put in the centre of the petri dish and the time for the tablet to completely disintegrate into fine particles was noted.

In-vitro Dissolution study

Dissolution of naproxen orodispersible tablets was carried out by using USP Dissolution apparatus Type II in 900 ml phosphate buffer pH 6.8 for 10 minutes. Samples were taken for 10 min and analysed using UV spectrophotomer at λmax 273.

3. RESULTS AND DISCUSSIONS:

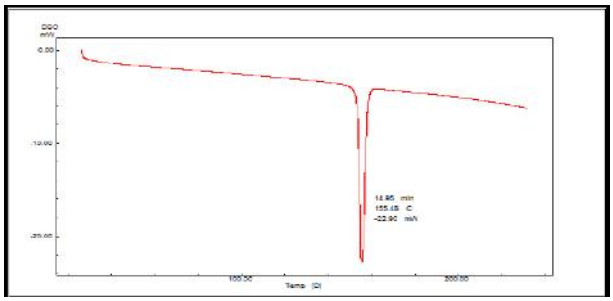

Fig 1: DSC of Naproxen Sodium

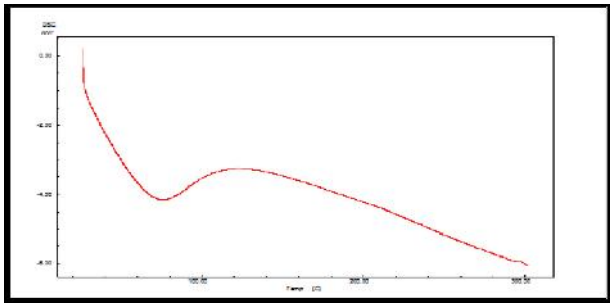

Fig 2 : DSC of Indion -234

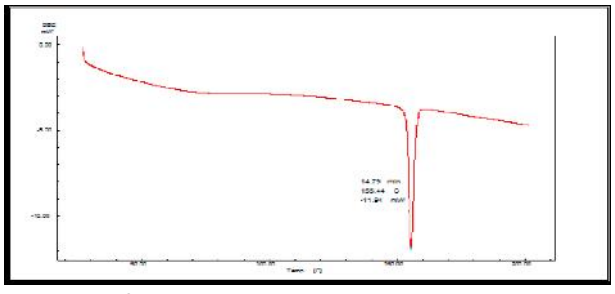

Fig 3: DSC of Resinate (Naproxen Sodium + Indion-234)

DSC indicates that Naproxen Sodium, Resin and Resinate containing solubilized agent exhibits endothermic peak at 155.44^0 C and 155.48^0 C respectively and thus it confirmed complex formation and no interaction was found between drug and resin.

Evaluation of Taste of Resinates:

Table 2: Bitterness level of resinates

Volunteer	BITTERNESS LEVEL AFTER					
	10sec	1min	2min	5min	10min	15min
1.	X	X	0	0	0	0
2.	X	0	0	0	0	0
3.	X	X	0	0	0	0
4.	0	0	0	0	0	0
5.	0	0	0	0	0	0
6.	0	0	0	0	0	0
7.	0	0	0	0	0	0
8.	0	0	0	0	0	0

3-Strong bitterness, 1-Slight bitterness, 0 - No bitterness, 2-Moderate bitterness, X-Threshold bitterness

Evaluation of Oro Dispersible Tablets

Table 3: Post compression studied of prepared orodispersible tablets

Formulation	Weight variation (mg) (±SD) (n=20)	Hardness (kg/cm^2) (±SD) n=3	Friability (%)	Disintegration time (sec) (±SD) n=6	Wetting time (sec) (±SD) n=3	Drug content (%) (±SD) n=10
F1	380±0.91	4.28±0.05	0.68	48±0.31	41.00±0.19	95.92±0.056
F2	381±1.23	4.31±0.06	0.65	40±0.55	32.33±0.11	99.26±0.065
F3	376±0.98	4.26±0.04	0.72	35±0.041	30.33±0.09	99.43±0.058
F4	379±0.42	4.23±0.07	0.82	39±0.49	25.43±0.07	98.54±0.087
F5	382±1.24	4.00±0.14	0.62	36±0.21	16.13±0.04	96.49±0.107
F6	378±0.41	4.22±0.11	0.85	21±0.39	19.53±0.12	98.22±0.452
F7	382±1.24	4.20±0.13	0.81	28±0.43	21.45±0.22	98.61±0.080
F8	379±0.43	4.33±0.04	0.88	30±0.36	23.66±0.20	97.57±0.077

In-vitro drug release study

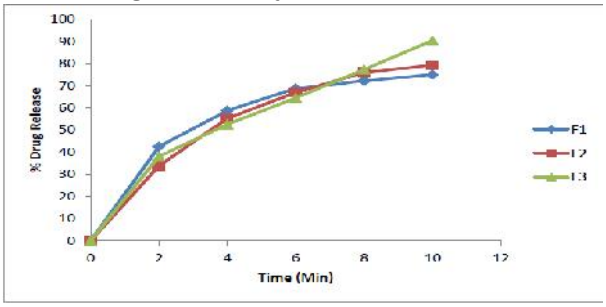

Fig 4: % Drug release F1-F3 batches

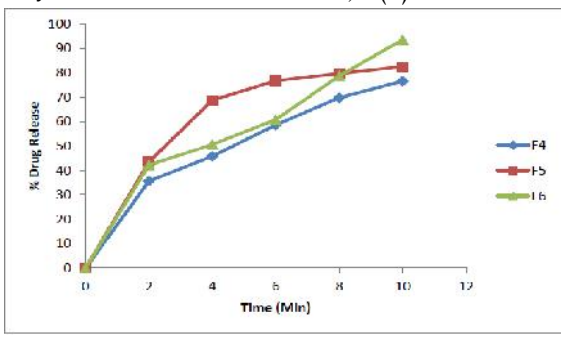

Fig 5: % Drug release F4-F6 batches

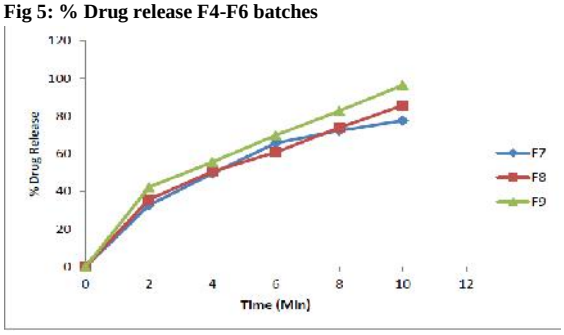

Fig 6: % Drug release F7-F9 batches

3^2 Factorial Design: Response data for all the 9 experimental runs of 3^2 factorial design carried.

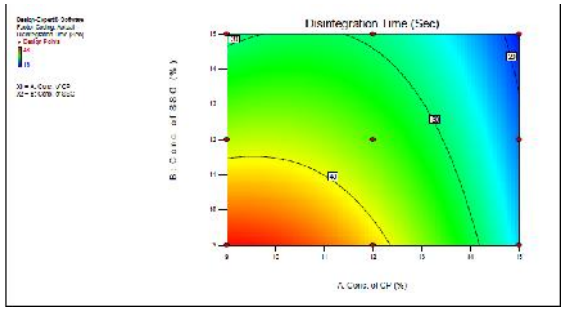

Fig 7: Contour Plot Showing the Effect of CP (X1) and SSG (X2) on Response Y1 (Disintegration Time)

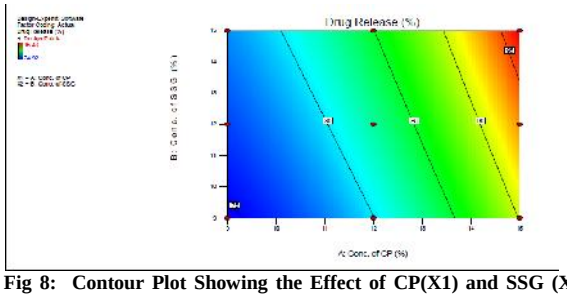

Fig 8: Contour Plot Showing the Effect of CP(X1) and SSG (X2) on Response Y2 (% Drug Release)

Response Surface Plots:

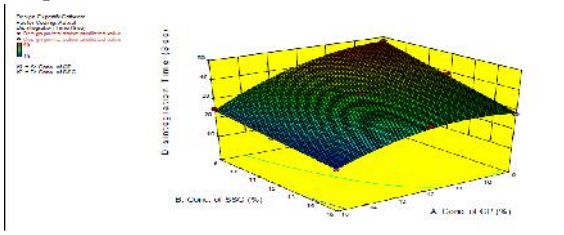

Fig 9: Response Surface Plot Showing the Effect of CP (X1) and SSG (X2) on Response Y1 (Disintegration Time)

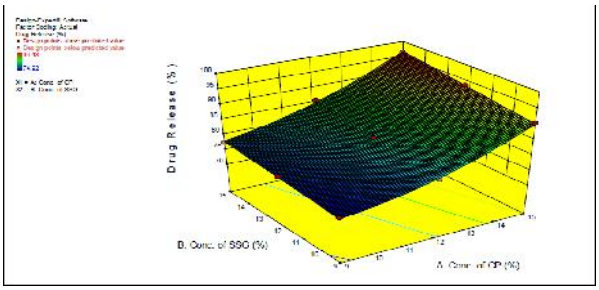

Fig 10: Response Surface Plot Showing the Effect of CP (X1) and SSG (X2) on Response Y2 (% Drug Release)

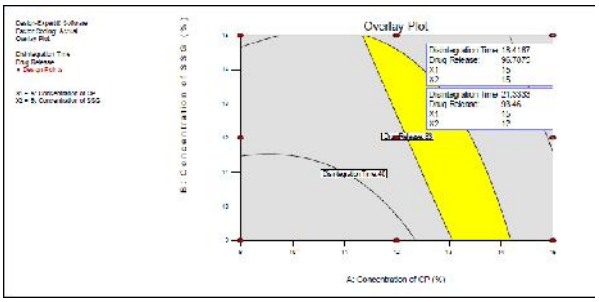

Fig 11: Overlay plot of CP and SSG

4. CONCLUSION

Naproxen sodium is non-steroidal anti-inflammatory drug; more than 50% of drugs are poorly soluble and bitter in taste. A success of formulation depends on how efficiently it makes the drug available at the site of action. Therapeutic effectiveness of a drug depends on the bioavailability and ultimately upon the solubility and taste of drug molecules especially in oral formulation. For improvement of taste of drug Ion exchange resin method is used. Then complex was characterized by DSC studies to check the drug-excipient interaction. The DSC thermogram indicates that Naproxen sodium, resin and resinate containing solubilized agent exhibits endothermic peak at 155.44^0 Cand 155.48^0 C respectively and thus it confirmed complex formation. 3^2 factorial design was employed to design orodispersible tablets. Out of nine formulations F9 was showed uniform friability, disintegration time (18 Sec) and % Drug Release (96.43%) in 10 min.

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