ORIGINAL RESEARCH ARTICLE

Formulation development of directly compressed Naproxen SR tablet using Kollidon SR and Avicel PH 102 polymer

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ABSTRACT

Naproxen is a well-known non-steroidal anti-inflammatory drug (NSAID). This work has been done for developing a formulation of 280 mg sustained release (SR) tablet where 150 mg active pharmaceutical ingredient (Naproxen) were used along with other excipients like Kollidon SR, Avicel PH 102, Lactose MH, Povidone K 30 and Mg-Stearate. Naproxen SR tablet was prepared by direct compression method aiming to enhance its dissolution properties. The physical parameters (hardness, thickness, diameter, average weight and friability) and drug release profile of this tablet were evaluated. The hardness of tablets from F1 and F2 formulation were highest and rest of them was also satisfactory. F2 formulation did not meet the friability test. But rests of the formulations were acceptable which indicate that others formulations can handle pressure during storage, transportation and packaging. All the formulations released 90% of drug within 120 minutes except F4 formulation. Among the six formulations, release was prompt in F1 formulation because of usage of higher concentration of polymer Kollidon SR. The outcome of this study indicates that the rate of dissolution of Naproxen SR tablet can be considerably improved with Kollidon SR.

Key Words: Non-steroidal anti-inflammatory drug, Naproxen, sustained release, direct compression, formulation, Kollidon SR.

INTRODUCTION

Naproxen (S)-6-methoxy-α-methyl-2-naphthalene acetic acid, is a widely used non-steroidal anti-inflammatory drug in the treatment of rheumatoid arthritis. It has been used for a long time because of its efficacy and safety profile (Ahmed *et al.*, 2010). This drug is recognized to be highly effective and clinically safe, but some side-effects such as gastrointestinal toxicity, nephrotoxicity, jaundice and hepatotoxicity have been reported (Hiroyuki *et al.*, 2006). This drug may rarely cause severe (rarely incurable) bleeding from the stomach or intestines. Older adults may be at higher risk for this effect (Aronson et al., 2010).Naproxen is used to relieve pain from various conditions such as headaches, muscle aches, tendonitis, dental pain and menstrual cramps. It also reduces pain; swelling and joint stiffness caused by arthritis, bursitis and gout attacks. It works by blocking body's production of certain natural substances that cause inflammation (Manrique-Moreno *et al.*, 2010). Development of sustained release oral dosage forms is beneficial for optimal therapy in terms of efficacy, safety and patient compliance. Ideally, a controlled release dosage form will provide therapeutic concentration of the drug in the blood that is maintained throughout the dosing interval (Javadzadeh *et al.*, 2008). The present study investigates the formulation of directly compressed SR tablets of Naproxen, by using a combination of polymers (Kollidon SR and Avicel PH 102). Kollidon SR is a free-flowing non hygroscopic powder consisting of polyvinyl acetate (80%, w/w) and polyvinylpyrrolidone (20%, w/w) combined as a physical mixture. It has a unique character of maintaining tablets geometric shape until the end of dissolution test, this is mainly due to its major component; the water insoluble polyvinyl acetate, while the minor water soluble part;

polyvinylpyrrolidone, is responsible for pore formation causing diffusion controlled release mechanism (Sark *et al.*, 2010). Avicel PH-102 is reported to exhibit better flow. The denser version of PH 101, PH 102, PH 301 and PH 302, respectively has improved flow property but reduce compressibility. Avicel PH 102 exhibited lower crushing strength and shorter disintegration time than Avicel PH 101 (Gad, 2008). In this study, an attempt was made to formulate directly compressed Naproxen sustained release tablet by using Kollidon SR and Avicel PH 102. The physical parameters (hardness, thickness, diameter, average weight and friability) and drug release profile of this tablet were evaluated.

MATERIALS AND METHODS

Formulation

The formulation of directly compressed Naproxen SR tablet was developed in this study. The ingredients used in the formulation are listed in table 1 along with justification of uses of each ingredient.

Direct compression method

It is known as direct compression because direct compression consists of compressing tablet directly from powder material without modifying the physical nature of the material itself (Beringer *et al.*, 2005). This method does not require any type of granulation either dry or wet granulation. Here drug, binder, diluents, lubricant are directly compressed by compression machine. Tablet production by direct compression involves only two operations in sequence, powder mixing and tableting. The advantage with direct compression is primarily a reduced production cost (Aulton, 2007).

Evaluation of formulated tablets

Average weight

Randomly, 20 tablets were selected after compression from each formulation and the mean weight was determined. None of the tablets deviated from the average weight by more than ±7.5% (USPXX). The USP has provided

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Table 1: Formulations of Naproxen SR tablets.

Ingredients	Justification of use	Amount of ingredients (in mg/tablet)					
		F1	F2	F3	F4	F5	F6
Naproxen	API	150	150	150	150	150	150
HPMC 15cps	Binder	28	33.6	39.2	44.8	50.4	56
Kollidon SR	Polymer	28	22.4	16.8	11.2	5.6	0
Povidone K30	Polymer	11.2	11.2	11.2	11.2	11.2	11.2
Avicel PH 102	Polymer	36	36	36	36	36	36
Lactose MH	Diluent	24	24	24	24	24	24
Mg-stearate	Lubricant	2.8	2.8	2.8	2.8	2.8	2.8
	Total =	280	280	280	280	280	280

Table 2: Physical properties of Naproxen SR tablets.

Properties	F1	F2	F3	F4	F5	F6
Thickness (mm)	3.3	3.4	3.4	3.5	3.4	3.4
Diameter (mm)	10.5	10.5	10.4	10.4	10.4	10.4
Hardness (kg/cm²)	6.8	6.8	5.9	4.4	5.3	4.9
Average Weight (mg)	279.1	278.6	275.2	277.2	277.1	275.2
Friability (%)	0.8	1.1	0.8	0.2	0.8	0.4
%Drug release	93.9	90.0	84.4	83.4	82.4	81.4

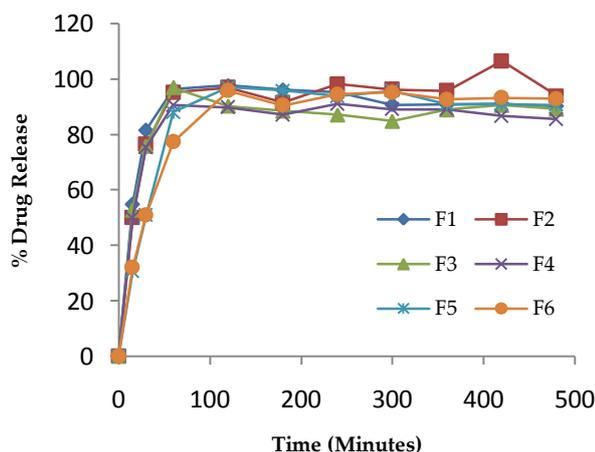All readings are average of 3 samples

Figure 1: Drug release profile of all formulations (F1-F6) of Naproxen SR tablet.

tolerances for the average weight of uncoated compressed tablets. These are applicable when the tablet contains 50mg or more of the drug substance or when the latter comprises 50% or more, by weight, of the dosage form.

Hardness test
Ten tablets of each of the formulations were taken and hardness was measured using a Monsanto hardness tester. The average value was calculated (Marshall *et al.*, 1987).

Thickness test
Ten tablets of each of the formulations were taken and thickness was measured by thickness tester and average was calculated.

Friability test
Ten tablets of each of the formulations were weighed out and taken into the rotating disk of a friability tester. It was allowed to rotate at 25 rpm for 4 minutes (100 revolutions). At the end of the rotation, tablets were collected, dedusted and reweighed. The friability was calculated as the percent of weight loss (Lachman *et al.*, 1990):

$$\text{Friability} = \frac{\text{Weight Loss}}{\text{Initial Weight}} \times 100$$

Dissolution test
The dissolution test of the formulated tablets was done by paddle method. Agitation is provided by a rotating paddle and the dosage form is allowed to sink to the bottom of the dissolution vessel before agitation is commenced. The dissolution medium should be 0.1M HCL and pH 7.4 buffer to stimulate the biological extremes according to USP, 2004 (Asian edition).

RESULTS AND DISCUSSION

The tablets from different formulations (F1-F6) were evaluated for hardness, thickness, diameter, average weight and friability and drug release profile. The results of these physical parameters summarized in the table 2. All the results calculated from average tablet samples. Thickness, hardness and average weight of all tablet formulations were found to be satisfactory. All formulation passed friability test except formulation F2. More than 90% of drug released within 120 minutes for all tablet formulation except F4 formulation. Drug release profile of Naproxen SR tablet presented in the Figure 1. Percent dug release against time was depicted in the figure. It was observed that drug release was prompt in case of F1 formulation because of higher concentration of polymer Kollidon SR was used in this formulation. This indicates that release of drug from Naproxen SR tablet is polymer dependant.

CONCLUSION

In this study direct compression method was used to prepare Naproxen SR tablet to increase their dissolution rate. For this purpose polymer Kollidon SR were used in different proportion in the formulation to see how it affects drug release profile. Physical parameters hardness, thickness and average weight of tablets of different formulations were evaluated and showed satisfactory results. F2 formulation does not meet the friability test but rests of the formulations were good enough which indicate that others formulations can handle pressure during storage, transportation and packaging. Among six formulations, release of F1 formulation was prompt because polymer Kollidon SR was used in higher concentration in this formulation.

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