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Research Article

PREPARATION AND EVALUATION OF SUSTAIN RELEASE INDOMETHACIN TABLETS USING SKIMMED MILK AND POVIDONE

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ABSTRACT

Inomethacin, a non steroidal anti inflammatory drug (NSAID) and COX inhibitor is a water insoluble drug. In order to improve its dissolution rate it was mixed with powder obtain from skimmed milk and granulation was performed of the same using POVIDONE of various grade.

The skimmed milk powder was used to overcome the side effect of inomethacin i.e. gastric disturbance. There was improvement in the dissolution but it was different in each i.e. the dissolution was higher in the low viscosity grade of inomethacin compare to the higher viscosity grade of POVIDONE. The analysis was carried out using double beam UV spectrophotometery.

Keywords: Inomethacin, granulation, skimmed milk, dissolution

INTRODUCTION

Inomethacin1-(4-chlorobenzoyl)-5-methoxy-2- methylindol-3-ylacetic acid., a non steroidal antiinflammatory drug (NSAID) and COX inhibitor,it is used for relief of symptoms of arthritis,primary dysmenorrhea, fever, and as ananalgesic. Like many other NSAID Inomethacin is practically insoluble in water. The poor solubility and wettability of Inomethacin leads to poor dissolution and hence variation inbioavailability. Thus increasing the dissolution isof therapeutic importnce.A large number of research had been carriedout to improve the dissolution rate. Various technique like spray drying, solid dispersion,use of polymer like cyclodextrin had been employed to enhanced the dissolution. POVIDONE one of the promising polymer both at research level as well commercial level was used for this particular study in order to improve its dissolution rate.In this study skimmed milk is used due to its surface active agent and amino acid content.Additionally, the milk is proposed against gastric disturbance caused by NSAID.

MATERIALS AND METHODS

Material: Skimmed milk (5%) was procured from Rampura diary and milk producer.Co-op (Kakanpur, Godhra, Gujarat).The Inomethacin was obtained as a gift sample from Shreya pharmaceutical Aurangabad and all other chemical and solvent were of analytical grade.

Methods

Preparation of skimmed milk

1000 ml of skimmed milk was evaporated at 35°C for 10 hrs and the dried powder was dried in an oven and passed through sieve no 80 and stored in an air tight container till further use. Preparation of granules using Povidone. Povidone was used to perform the granulation. Inomethacin and dry milk powder was mixed together and was passed through sieve no 40 for carrying out dry mixing. 10 % of Povidone solution dissolved in water was used as the binding agent(Table1,2and3).

Table 1: Formulation 1

Sr no	Ingredients	Qty per tab (mg)	Qty per 20 tab (mg)
1)	Skimmed milk powder	100	2000
2)	Inomethacin	50	1000
3)	POVIDONE	50	1000
4)	Starch	25	500
5)	Mg Stearate	05	100

Table 2: Formulation 2

Sr no	Ingredients	Qty per tab (mg)	Qty per 20 tab (mg)
1)	Skimmed milk powder	100	2000
2)	Inomethacin	50	1000
3)	POVIDONE	100	2000
4)	Starch	25	500
5)	Mg Stearate	05	100

Table 3: Formulation 3

Sr no	Ingredients	Qty per tab (mg)	Qty per 20 tab (mg)
1)	Skimmed milk powder	100	2000
2)	Inomethacin	50	1000
3)	POVIDONE	150	3000
4)	Starch	25	500
5)	Mg Stearate	05	100

As mention in above table the various proportion POVIDONE of various grade were utilize to prepare the granules. The viscosity plays a very important in release of the drug from the formulation. So the main aim to use low viscosity grade was to improve the dissolution of the drug. Granulation was perform by dry binding technique.

Preparation of tablets

Inomethacin and skimmed milk powder weighed and passsed through 60. Starch was added to the above blend. POVIDONE was dissolved in water and was added to above mixture as a binder. The granules were formed by wet granulation method. The granules formed were passed through sieve no 40 and dried in tray dryer for 2 hr at 60°C. The lubrication were was done using Mg Stearate. The granules were compressed using 10 station tablet rotary press.

Dissolution studies

The dissolution study was carried out using 900 ml of *phosphate buffer pH 7.2* as the medium and rotating the paddle at 100 rpm for 12 hours. Withdraw a suitable volume of the sample and filter promptly through a membrane filter disc with an average pore diameter not greater than 1.0 mm. Reject the first few ml of the filtrate and dilute a suitable volume of the filtrate with the same solvent. Measure the *absorbance* of the resulting solution at the maximum at about 320 nm.

RESULTS AND DISCUSSION

It was seen that all the three formulation were able to release the drug upto 12 hr but the release of the drug from the tablet was varying in all the three formulation.

In formulation 1 the release was upto 97 %, in formulation 2 it was upto 93 % whereas in formulation 3 it was upto 57 %. The dissolution profile and the release pattern is shown in given below table and figure. The tablets also complied with the hardness and friability test.

Table 4 Dissolution profile for formulation 1

Time (hrs)	%CR
0	0
1	10.5
2	15.5
3	23.4
4	27.5
5	32.6
6	38.2
7	40.6
8	50.0
9	52.0
10	56.9
11	70.9
12	97.5

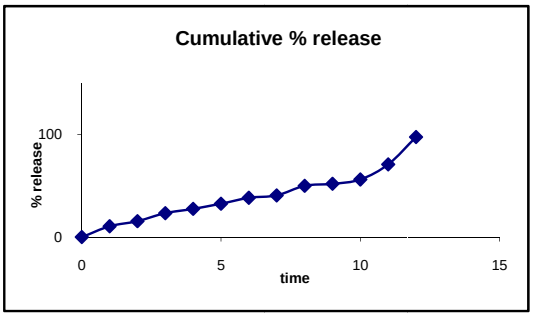

Fig. 1 Dissolution pattern for formulation 1

Table 5: Dissolution profile for formulation 2

Time (Hrs)	Cum % rel
0	0
1	20.703
2	22.026
3	31.963
4	42.860
5	47.627
6	55.287
7	64.649
8	92.938
9	93.446

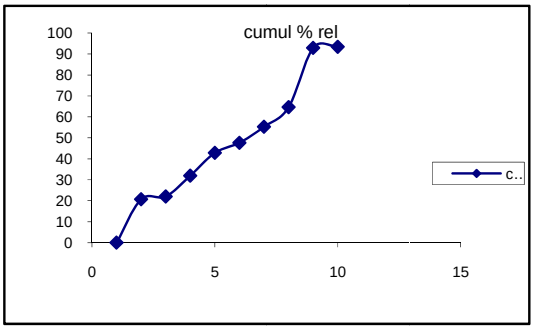

Fig. 2: Dissolution pattern for formulation 2

Table 6: Dissolution profile for formulation 3

Time (Hrs)	Cumul % rel
0	0
1	6.2
2	10.0
3	14.7
4	18.0
5	23.0
6	28.5
7	30.0
8	35.8
9	42.8
10	45.6
11	57.8

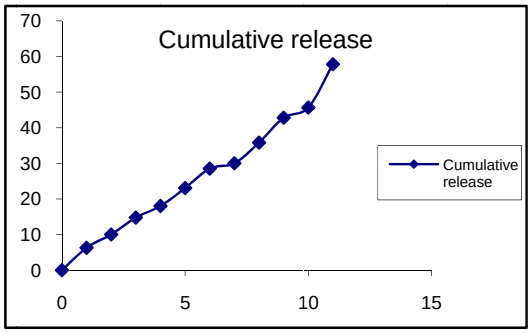

Fig. 3: Dissolution pattern for formulation 3

1. As seen from the above table there was large variation in all the three formulation.
2. The drug release from the formulation 1 was highest compare to formulation 2 and formulation 3.
3. The reason for this must be the low viscosity of the polymer used that is POVIDONE.
4. Also from the literature it was studied that more viscosity tend to retard the release of the drug from the formulation.
5. One more important the thing which was noticed during the formulation was that the appearance of the tablet was very good.
6. Hence from the formulation it was concluded that all the formulation were successfully design but the cumulative percent release was observed in the formulation 1.

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