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DEVELOPMENT OF ENTERIC COATED TABLETS OF IBUPROFEN USING METHACRYLIC ACID COPOLYMER

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ABSTRACT

In the present research paper, anti-inflammatory enteric coated ibuprofen tablets were prepared using PVPK-30 and starch as disintegrating agents. Methacrylic acid copolymer was used as an enteric coating material. The tablets were formulated using wet granulation method. Further *in vitro* drug release from ibuprofen enteric coated tablets were studied using different percentage of coating material utilizing different dissolution mediums. The results suggested that the prepared enteric coated tablet is an excellent candidate for colon specific drug delivery. Moreover, to achieve the maximum drug release coating of 7% is desired.

INTRODUCTION

Ibuprofen is a nonsteroidal anti-inflammatory drug[1] (NSAID), which relieves pain and inflammation. It is used in the treatment of headaches, muscle aches, backaches, dental pain, arthritis, menstrual cramps and athletic injuries[2-3]. The medication containing ibuprofen is also used to reduce fever and minor aches and pain due to the common cold and flu. Chemically it is (*RS*)-2-(4-(2-methylpropyl)phenyl)propanoic acid (Figure 1) with the bioavailability in the range of 49-73%. The protein binding ability of this drug is usually very high i.e. around 99%.

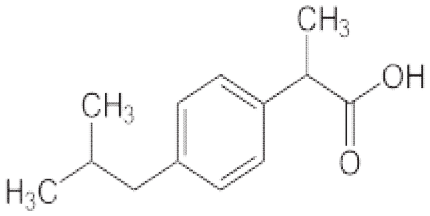

Figure 1: Chemical Structure of Ibuprofen

The drug under this category usually works by blocking the enzyme in the body that makes prostaglandins (PG). Ibuprofen work by inhibiting the enzyme cyclooxygenase (COX), which converts arachidonic acid to prostaglandin H_2 (PGH_2). Some other enzymes in turn convert PGH_2 to several other prostaglandins and to thromboxane A_2. Thromboxane A_2 stimulates platelet aggregation, leading to the formation of blood clots. Decreasing prostaglandins helps to reduce pain, swelling and fever. Ibuprofen is known to have an antiplatelet effect due to the formation of thromboxane A_2, though it is relatively mild and short-lived when compared with other better-known antiplatelet drugs[4-5]. Ibuprofen also acts as a vasodilator, helps in the dilation of coronary arteries and some other blood vessels. WHO model list of essential medicines has listed this drug as a core medicine[6].

As far as the literature goes the number of evidence can be spotted for the formulation, development and evaluation of the enteric coated drug formulations [7-12]. Kannan et al.[13] prepared Aspirin delayed release tablet and evaluated the parameters like half life, disintegration etc. using micro crystalline cellulose, maize starch, cross carmilose sodium. Henry Zhao et al.[14] developed a robust two-step dissolution test for enteric-coated immediate- and extended-release solid oral dosage formulations with fast HPLC analysis. Kumar et al.[15] formulated enteric coated

Esomeprazole magnesium trihydrate tablets using direct compression and enteric coated with Acryl EZE. The parameters like compressibility, hardness and flow behavior were also studied. The compression parameters after enteric coating were found to be uniform and consistent. Kakuta et al.[4] specified that cyclooxygenase-1-selective inhibitors are attractive candidates for analgesics that do not cause gastric damage. This makes these drugs an efficient candidate for colon specific drug delivery.

MATERIAL AND METHODS

Materials

Ibuprofen was a gifted sample provided by Boots India Limited, Mumbai. Methacrylic Acid Copolymer (Signet labortaries, Mumbai) was used as received. All other chemicals used were of analytical grade and were used as received. UV-VIS analysis of sample was carried out on Systronics UV-VIS spectrophotometers.

Methods

Preparation of Enteric coated tablets of Ibuprofen was done by wet granulation method. Methacrylic Acid Copolymer (Signet labortaries, Mumbai) was used to coat the prepared tablet in order to make the tablet enteric coated. Table 1 represents the formulation of enteric coated tablets.

Table 1: Composition of IBUPROFEN tablets 400 mg

S. No.	Active drug with excipients	Amount/1000 tablets (in gm)
1	Ibuprofen	400.00
2	Starch (maize)	48.45
3	Povidone (PVPK-30)	18.00
4	Starch (Maize)	108.13
5	Starch (Maize dried)	40.00
6	Aerosil (Colloidal Silicon Dioxide)	4.00
7	Aerosil (Colloidal Silicon Dioxide)	3.45
8	Stearic acid	1.50
9	Magnesium Stearate	4.50
10	Purified Water	163.97

Colon specific drug release

a) In vitro drug release from ibuprofen enteric coated tablets

The tablets were coated with different percentage (4%, 5%, 6% and 7% respectively) of coating material. The six tablets for each type were evaluated for *in vitro* drug release. The tablets were subjected to *in vitro* drug release for 24 hours in a calibrated USP dissolution test apparatus equipped with paddles employing 900 ml phosphate buffer (pH 6.4, mimicking conditions of ascending colon). The paddles were rotated at 50 rpm. The dissolution media was maintained at a temperature of 37 ± 0.5 ^{o}C. Samples (2 ml) were withdrawn and analyzed spectrophotometrically at 221 nm employing UV-Vis spectrophotometer after suitable dilution of the samples. The fresh dissolution medium was replaced after each withdrawal. The percentage of ibuprofen released over time was calculated using following formula.

$$\%\text{Dissolution} = \frac{\text{Samples absorption}}{\text{Standard Absorpton}} \times \frac{\text{standard weight}}{100} \times \frac{1}{100} \times \frac{900}{1} \times \frac{100}{2} \times 0.991 = y$$

$$\%\ \text{dissolution} = \frac{Y \times 100}{\text{Claim}}$$

The samples were collected at different time intervals of 2, 8, 12, 16, 20, 24 hrs respectively.

RESULTS AND DISCUSSION

Different type of dissolution mediums were used for the evaluation of the enteric coated tablets.

Table 2: Percentage dissolution with 4% coating

Dissolution media	Time in Hours	1st tablet	2nd tablet	3rd tablet	4th tablet	5th tablet	6th tablet
Simulated Gastric Fluid	2	76.53	78.59	76.84	78.45	77.18	75.94
Simulated Intestinal fluid	4	95.32	96.27	95.82	96.22	94.85	94.98
Simulated Colonic Fluid	6	99.04	99.28	99.16	98.75	98.51	98.68
	8	97.35	98.59	97.99	97.19	97.84	97.86
	12	96.87	97.61	96.81	95.37	96.83	96.11
	14	93.48	93.85	93.66	93.12	93.74	93.54

Table 3: Percentage dissolution with 5% coating

Dissolution media	Time in Hours	1st tablet	2nd tablet	3rd tablet	4th tablet	5th tablet	6th tablet
Simulated Gastric Fluid	2	69.39	69.00	68.61	69.52	69.65	69.14
Simulated Colonic Fluid	6	82.54	82.87	83.10	82.36	82.88	82.99
	8	93.04	93.16	94.27	93.53	93.78	93.29
	12	98.22	98.74	99.13	98.61	98.87	99.13
	14	94.96	94.92	94.83	94.70	94.22	94.97
	18	92.87	92.48	92.22	92.61	92.87	92.00

Table 4: Percentage dissolution with 6% coating

Dissolution media	Time in Hours	1st tablet	2nd tablet	3rd tablet	4th tablet	5th tablet	6th tablet
Simulated Gastric Fluid	2	49.43	49.36	49.19	49.69	50.11	49.86
Simulated Colonic Fluid	8	67.85	68.39	68.22	68.03	67.95	68.49
	12	83.59	83.37	83.15	83.70	83.81	83.37
	16	96.07	96.45	96.20	96.81	96.57	96.20
	18	99.48	99.35	99.61	99.22	98.97	98.84
	20	94.72	94.37	94.88	94.50	94.24	94.37
	24	91.54	91.48	91.78	91.46	91.75	91.44

Table 5: Percentage dissolution with 7 % coating

Dissolution media	Time in Hours	1st tablet	2nd tablet	3rd tablet	4th tablet	5th tablet	6th tablet
Simulated Gastric Fluid	2	38.68	38.68	38.42	39.46	39.73	39.20
Simulated Colonic Fluid	8	59.87	59.21	59.47	59.21	63.26	58.95
	12	82.79	82.35	82.24	82.57	82.35	82.68
	16	94.44	96.27	94.14	94.15	94.02	93.89
	20	97.55	98.45	97.29	97.12	97.29	96.90
	24	98.59	98.72	100.63	98.88	98.34	98.34

The dissolution testing of enteric coated tablets confirms that the coating material used for preparation of the ibuprofen tablets is specific for colon targeting. Moreover, the maximum colonic drug delivery can be achieved by use of the enteric coating of 7 %.

CONCLUSION

From the ongoing studies, it was concluded that, Ibuprofen enteric coated tablets prepared by wet granulation techniques, showed promising results. Methacrylic Acid copolymer prevents the release of drug for the first 2hrs. The enteric coated tablets are economical and exhibit predictable release behavior. Moreover, with the specified percentage of coating material of 7% maximum release can be effectively achieved. The coating with copolymer and nonselective COX inhibitor properties makes the formulation an excellent candidate for colon specific drug delivery.

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