



International Journal of Biological & Pharmaceutical Research

Journal homepage: www.ijbpr.com

IJBPR

COMPARATIVE STUDY OF ENTERIC COAT POLYMERS IN DELAYED RELEASE SULFASALAZINE TABLET

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ABSTRACT

The main aim of the work is to develop delayed release enteric coated tablet formulation of Sulfasalazine using different enteric coat polymer. Sulfasalazine delayed release tablet is used to increase bioavailability and to prevent acid degradation, delivering the drugs to its local site of action in the intestine. Core tablets of Sulfasalazine were prepared and evaluated. The cellulose acetate phthalate, HPMC-P polymers were used to coat the core tablet. On the basis of weight gain and USP specification the tablets were coated. The design of enteric coating based on the transit time required for passage to the intestine and may be accomplished through coatings of sufficient thickness. In general these substances are anionic polymers or copolymers which are insoluble in acidic media but acquire water solubility at near neutral pH values due to ionization of functional groups along the polymer chain. The application of enteric coat in combination gives more satisfactory & desired effect. Due to combination, the enteric coat may have high cohesive and adhesive forces of attraction between the functional group. It is concluded that, the enteric coat polymer gives promising dosage form to target the organ and prevent the loss of drug.

Key Words: Delayed release tablet, Enteric coating tablet, Hydroxy propyl methyl cellulose, Cellulose acetate phthalate, Hydroxy propyl methyl cellulose phthalate (HPMCP).

INTRODUCTION

The tablet dosage form is the most popular and successfully used for oral drug administration. It is probable that almost 90% of all the drugs are administered by oral route including tablet form. It is the one of an essentially tamper proof dosage form containing drug with or without suitable diluents and usually obtained by comprising uniform volumes of particles containing powders or granules (Aulton ME, 2002). A delayed-release dosage form is designed to release the drug at a time other than promptly after administration. Tablet specially coated to remain intact in the stomach to yield their ingredients in the intestines are termed enteric coated. The most common

type of delayed-release tablet is an enteric coated tablet, for which the drug is released in the upper part of the small intestine after the preparation has passed the stomach (Budavari S *et al.*, 2007). Sulfasalazine, gastrointestinal & anti-inflammatory agent which is combination of sulfonamides (Sulfapyridine) with a salicylate. It is used in Crohn's disease, ulcerative colitis & rheumatoid arthritis. It is split into its component parts by bacteria in the colon, the 5-amino salicylic acid being the putative radical scavenger responsible actual therapeutic activity (Graham C *et al.*, 2008; Lachman L *et al.*, 2008). A delay release enteric coated tablet of Sulfasalazine resists the acidic environment of the stomach & to disintegrate in the higher pH environment of intestinal fluid. Various pH dependant polymers such as CAP, HPMCP and combination of both are used for this tablet which degrades in intestinal pH.

The aim of present work is to develop delay release enteric coated tablet formulation of Sulfasalazine to increase bioavailability, prevent acid degradation, to

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reduce gastric irritation & delivering the drugs to its local site of action in the intestine.

MATERIALS AND METHODS

Sulfasalazine, HPMC and Cellulose acetate phthalate was obtained as a gift sample from Wallace Pharmaceuticals, Karnataka. WINCOAT (HPMC-P) obtained as a gift sample from Leben Pharmaceuticals, Akola. The other ingredients were used are of analytical grade.

Differential scanning Calorimetry (DSC) study

Thermograms were obtained by using a differential scanning calorimeter (DSC Q20 V24.4 Build 116, Japan) at a heating rate 10°C/min over a temperature range of 0-300° C. The sample was hermetically sealed in an aluminium crucible. Nitrogen gas was purged at the rate of 10 ml/min for maintaining inert atmospheres. DSC of Sulfasalazine, CAP, and WINCOAT in single and combinations were studied.

Preparation of Sulfasalazine Core Tablets

The core tablet containing Sulfasalazine was prepared by wet granulation method. The compositions of core tablet are mentioned in table 1. Fluidized bed dryer is used to maintain the loss on drying. These blended materials were compressed in oval shape.

Evaluation of core tablets

The prepared core tablet was subjected to different physical evaluation including drug content and disintegration test. The only optimized batch of core tablet was considered for further study.

Formulation of seal coating solution

Seal coating was applied to core tablets to protect the drug from reacting with enteric coating and other environmental conditions as well as to facilitate proper uniformity of enteric coating material. HPMC as sealant and PEG 4000 as plasticizer in the 4:1 ratio in water were prepared as seal coating solution (Table 2). The 2 % seal coat was applied to core tablets of formulation F3.

Formulation of enteric coating solution

Enteric coating solutions as E1, E2, & E3 formulation using solvent acetone and isopropyl alcohol were prepared. The enteric coating polymer: PG ratio was 3:1 (Table 3). The coating of polymer on core tablets (F3) was done on weight gain basis (2%, 4%, 6%, 8% and 10 %). The table 4 indicates, the parameters used during seal coating process and enteric coating process.

In vitro dissolution study

In vitro drug release study for the prepared enteric coated tablets were conducted using USP XXIV type-II (Paddle) dissolution apparatus at 37±0.5°C with 100 rpm speed using 900 ml of 0.1N HCl as dissolution medium. A 5 ml sample solution was withdrawn from the dissolution apparatus at the end of the 2 hours and then media was changed into phosphate buffer pH 7.5. At the end of 1 hour 5 ml sample was withdrawn from acid media. After filtration and appropriate dilution, the samples were analyzed for Sulfasalazine by a HPLC-UV spectrophotometer at 254 nm.

RESULTS

Differential scanning Colorimetry (DSC) study

Table 1. Composition of Sulfasalazine core tablet.

S.No	Ingredients	Formulation code (amount in mg/tab)		
		F1	F2	F3
1.	Sulfasalazine	500	500	500
2.	Microcrystalline Cellulose	60	60	60
3.	Starch	64	64	64
4.	Sodium Starch Glycolate	05	10	15
5.	Poly Vinyl Pyrrolidone	14	14	14
6.	Talc	12	12	12
7.	Magnesium Stearate	06	06	06
8.	Sodium Lauryl Sulphate	04	04	04
9.	Total	665	670	675

Table 2. Composition of seal coating solution

Sr.No.	Name of polymer	Quantity (g)
1.	HPMC	8
2.	PEG 4000	2
3.	Water	185

Table 3. Composition of enteric coating solution

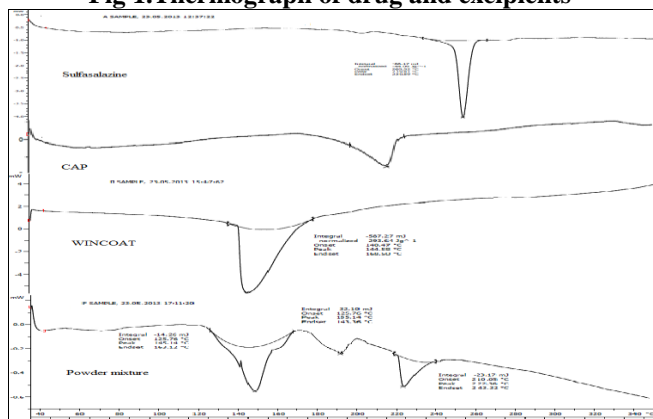
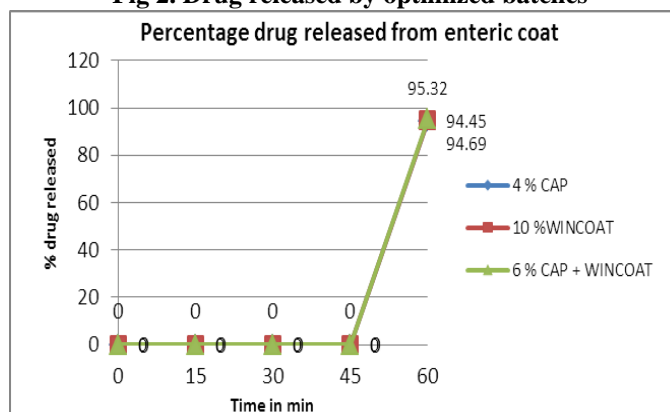
S.No.	Name of Polymer	Formulation Code (g)		
		E1	E2	E3
1.	Cellulose Acetate Phthalate (CAP)	3	-	-
2.	WINCOAT	-	3	-
3.	CAP + WINCOAT	-	-	1.5+1.5
4.	Propylene Glycol (PG)	1	1	1
5.	Acetone	20	20	20
7.	Iso Propyl Alcohol (IPA)	30	30	30

Table 4. Coating process parameters

S.No.	Parameters	Seal coating	Enteric coating
1.	Product temperature (0C)	32-34	29-31
2.	Fluid delivery rate (g/min)	5-6	4-5
3.	Pan speed (rpm)	16-18	13-15
4.	Atomization air pressure (bar)	1.5	1.5

Evaluation of core tablets**Table 5. Physical evaluation of Sulfasalazine core tablet**

S.No.	Parameters	Formulation code		
		F1	F2	F3
1.	Avg. wt of a tab. (mg)	665.5	669	675
2.	Thickness (mm)	5.20	5.10	5.38
3.	Hardness (kg/cm ²)	4.5	6.0	9.5
4.	Friability (%)	1.9	1.4	0.29
5.	Disintegration test (DM water)	12	8.5	4
6.	Drug content (%)	98.74	98.02	99.28

Fig 1. Thermograph of drug and excipients**Fig 2. Drug released by optimized batches****DISCUSSION**

The thermogram exhibited a sharp melting endotherm peak at 219.81°C for Sulfasalazine. DSC thermogram of polymer and excipients, which shown in figure 2, elucidate that there was not any major difference found between onset temperature and peak temperature, hence there was no interaction found between drug and polymer in physical mixture.

Evaluation of core tablets

The physical parameters of core tablets are mentioned in table 5. All the data complies with the standard. The formulation F1 and F2 batches were failed friability test, hence formulation F3 was considered optimized batch.

Seal coating

Seal coating was done upto 2% on core tablet on the basis of weight gain. 2% seal coating uniformity was

also evaluated by visual inspection. Satisfactory results of seal coating were observed.

Enteric coating and in-vitro dissolution of sealed coated tablets

On the basis of percentage drug released during first 2 hour in 0.1 N HCl, further coating on weight gain basis continued for failed batches till the zero percent drug released found in 0.1 N HCl. The passed tablets were subjected to dissolution study phosphate buffer pH 7.5 for 1 hour. As per the specification given in USP, in 0.1 N HCL, NMT 10% and in phosphate buffer pH 7.5, NLT 85% drug must release. In dissolution study four CAP coated tablets (out of six) with 2% weight gain were failed in 0.1 N HCL, and remaining two tablets, which passed the limit was further subjected to dissolution in phosphate buffer pH 7.5. The percent drug released by those tablets was 95.44 % & 98.40% (96.92 ± 2.09). All tablets of 4% & 6% weight gain were passed the acid stage, the percentage drug released was (94.45 ± 2.04) & (99.33 ± 2.24) for 4% and 6% weight gain respectively. With WINCOAT polymer, all six tablets of 2% & 4% weight gain were failed in 0.1 N HCl. In 6% weight gain, four tablets were failed and remaining two tablets which passed the limit was further subjected to dissolution in buffer stage. The percent drug released by these tablets was 92.37 % & 90.34% (91.35 ± 1.43). In case of 8% weight gain, three tablets failed and remaining three tablets were passed the acid stage. Acid stages passed 3 tablets were further studied for buffer stage and 95.33%, 91.22% & 94.33% (93.62 ± 2.14) drug release shown by those tablets. Finally, single tablet of 10% weight gain was failed the acid stage and remaining 5 tablets were subjected to buffer stage. The percent drug release was in range 98.53% to 98.27% (94.69 ± 3.37). In combinations of CAP + WINCOAT polymer with 4% weight gain, one tablet failed out of 6 tablets, in acid stage and remaining 5 tablets which passed the acid stage continued for buffer stage. The percent drug released by those tablets was ranges from 90.28%-99.18% (96.19 ± 3.39). In case of 6%, 8% & 10% weight gain, all 6 tablets were passed in acid stage which further subjected to buffer stage and given 95.32 ± 2.42 , 96.67 ± 1.86 & 94.81 ± 3.56 percent drug released.

The design of enteric coating based on the transit time required for passage to the intestine and may be accomplished through coatings of sufficient thickness. In

general these substances are anionic polymers or copolymers which are insoluble in acidic media but acquire water solubility at near neutral pH values due to ionization of functional groups along the polymer chain. Dissolution analysis was employed to assess the effect of the enteric coat composition and coverage levels on the release of the formulations.

Single use of CAP as enteric coat gives 97.07% (94.45 ± 2.40) release in formulation with coat of 4%. This may happened due to ionization of polymer in 0.1 N HCL & less thickness of coat (2%). While WINCOAT polymer as enteric coat upto 2% & 4% weight gain fails the tablet, because of less thickness and highly ionization of functional group. But on 10% weight gain, WINCOAT produce high thickness requires more time to dissolve. The maximum percentage drug release in 10% weight gain is 98.27 % (94.69 ± 3.37).

The application of enteric coat in combination gives more satisfactory & desired effect. Due to combination, the enteric coat may have high cohesive and adhesive forces of attraction between the functional group. Both CAP & WINCOAT gives synergistic effect with less weight gain at 6% drug released (95.32 ± 2.42) & at 8% may produce 99.21% (96.67 ± 1.86) drug release. As per limit gives in USP all the batches by CAP + WINCOAT were passed and released drug in 0.1 N HCL. But in combination of less weight gain, the formulation with 6% weight gain was continued as optimized batch which release 98.40% (94.81 ± 3.56) drug in 7.5 phosphate buffers.

CONCLUSION

Acid degradation, enzymatic degradation and hepatic degradation is one of the causes for low availability of drug into the biological system. Hence at last we conclude that the combination of CAP and HPMC-P have promising delay release property and can achieve higher bioavailability of drug. Enteric coat and polymer used generally dissolve by ionization of functional group. This can also help to ionize the drug molecule containing same functional group and increase the dissolution and absorption rate in colon targeted drug delivery system.

ACKNOWLEDGEMENT

Authors are thankful to Leben Pharmaceuticals, Akola & Shreya pharmaceuticals, Aurangabad, for providing gift sample from of drug and polymers.

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