Original Article

Formulation And Evaluation Of Tamarind Based Aceclofenac Extended Release Matrix Tablets

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DOI: 10.47750/pnr.2022.13.S08.619

Abstract

The present investigation is aimed at studying the applicability of tamarind gum in the design of extended release formulations of aceclofenac. PVP K30, a synthetic polymer was selected as binder. HPMC is taken as another polymer for comparison over the natural gum efficiency. Drug-excipient compatibility studies, pre-compression blend studies, tablet characteristics, in-vitro drug release and release kinetic studies were performed. Results indicated that all the blend and tablets characteristics are within the acceptable criteria. The drug release from the matrix tablets depended on the polymer concentration and increase in polymer concentration retarded the drug release effectively. HPMC polymer has shown better drug release control over the natural gum tamarind. However, the drug release was extended up to 24 hours with tamarind gum and the drug release followed zero order release kinetics with diffusion mechanism.

1. INTRODUCTION

A pharmaceutical dosage form is characterized by the presence of one or more active pharmaceutical ingredients and additives that are commonly referred as excipients[1]. Excipients used to control the release of active from a dosage form for extended period via diffusion and/or erosion mechanism, are commonly known as rate controlling polymers. Natural excipients are preferred over the synthetic excipients because they are generally inert, safe, non-toxic, biocompatible, biodegradable, low cost, eco-friendly and abundantly available in nature[2,3]. Natural polymers or "gums" have a huge history of utilization in various applications. Gums are usually obtained from plant bark exudates, seeds (soya bean), cereals (wheat and rice) seaweeds and microbial sources. A large number of plant families like, Leguminosae, Combretaceae and Stericuliaceae produce gums in lager quantity[4,5].

Natural gums have aroused remarkable interest due to their varied pharmaceutical application such as gelling, binding, thickening, stabilizing suspending, emulsifying, disintegrating, film forming, matrix forming, and release controlling properties[6].

The present investigation is aimed at studying the applicability of tamarind gum in the design of extended release formulations of aceclofenac. Tamarind gum is commonly available poly saccharide obtained from the dried kernels/seeds of the tree tamarind known as "imli" in the Indian sub-continent[7-10]. Aceclofenac is a nonsteroidal anti-inflammatory drug with anti-inflammatory, analgesic properties, and antipyretic activity, which acts by inhibiting the body's production of prostaglandins with low and rare side effects[11,12].

2. MATERIALS AND METHODS

A semisynthetic polymer hydroxyl propyl methyl cellulose K100M (HPMC K100M) was used to have comparable dissolution profiles with known polymer and to decide the levels of gum for desired drug release. PVP K30, a synthetic polymer was selected as binder[13]. UV spectroscopic method was selected for the *in vitro* estimation of aceclofenac in formulations and dissolution samples. UV spectrophotometric method of estimation of aceclofenac was based on the measurement of absorbance at 275 nm in pH 6.8 phosphate buffer[14].

2.1. Drug-excipient compatibility study

The compatibility studies were performed for drug-excipient physical mixtures. Drug and excipient mixtures were mixed properly in proportions of 1:3 and packed in amber glass vial and closed with elastomeric closure, then compatibility study was done by storing at different temperature conditions 40±2°C 75±5% relative humidity and 50±2°C for four weeks and evaluated after intervals of 2 weeks[15]. No relative humidity was considered for 50±2°C temperature conditions. For comparison, pure drugs and excipients were also stored under similar conditions and evaluated. After two week intervals, the samples were visually inspected for any physical changes by comparing with initial samples kept as control at ambient conditions and physical mixtures were tested for respective drug content and compared with respective initial drug content values. Drug content was estimated for respective drugs in samples in triplicate using UV assay method.

2.2. Preparation and evaluation of aceclofenac matrix tablets using tamarind gum

2.2.1. Preparation of precompression blend and tablets

The dose of aceclofenac was kept as 200 mg/tablet[16]. Extended release matrix tablets were prepared by wet granulation method. The composition of the prepared tablets is shown in **Table 1**. The final blend was compressed into tablets on a 16-station rotary punching machine (M/s. Cadmach Machinery Co. Pvt. Ltd., India) using 10.5 mm round flat faced punches.

2.2.2. Evaluation of precompression blend for flow properties

The powder blends of all formulations were evaluated for flow properties angle of repose, Carr's index (CI) and Hausner's ratio (HR). All these trials are made in triplicate and average values were calculated.

Table 1: Composition of aceclofenac tablets for initial screening

Ingredient (mg)	AH1	AH2	AH3	AH4	AH5	AT1	AT2	AT3	AT4	AT5
Aceclofenac	200	200	200	200	200	200	200	200	200	200
HPMC	20	90	160	230	300	-	-	-	-	-
Tamarind gum	-	-	-	-	-	20	90	160	230	300
PVP	20	20	20	20	20	20	20	20	20	20
Lactose monohydrate	300	230	160	90	20	300	230	160	90	20
Magnesium stearate	10	10	10	10	10	10	10	10	10	10
Tablet weight (mg)	550	550	550	550	550	**550**	**550**	**550**	**550**	**550**

2.2.3. Evaluation of matrix tablets

Compressed tablets were evaluated for tablet properties of thickness, hardness, friability, uniformity of weight and percent drug content[17].

2.2.4. *In vitro* dissolution studies

Drug release from the matrix tablets of aceclofenac[18,19] and was studied using USP type I (basket) dissolution apparatus, in 900 mL of pH 6.8 phosphate buffer at 37±0.5ºC at 75 rpm. 5 mL of dissolution medium was withdrawn using a syringe fitted with 0.45 µm pre filter at regular time intervals and the same volume of fresh dissolution medium maintained at 37±0.5ºC was replaced. The cumulative percent of drug released at different time intervals was calculated.

2.2.5. Drug release kinetics and mechanism

The rate and mechanism of drug release play an important role in assessing the quality of the dosage form and also for achieving the desired time of drug action in the body for controlled release dosage forms. The drug release kinetics was evaluated by fitting the data to zero and first order[20,21]. Mechanism of drug release was evaluated by fitting the data to Higuchi diffusion model, erosion model and further characterized by using Korsmeyer-Peppas equation[22-25].

3. RESULTS AND DISCUSSION

3.1. Drug-excipient compatibility study

No significant physical change was observed including color in all samples after 4th week. The drug content also remained unchanged compared to initial sample after 4th week indicating no degradation of aceclofenac with the excipient mixtures studied.

3.2. Evaluation of precompression blend for flow properties

The angle of repose values were in the range of 31-34° while CI was between 10 and 15. Hausner ratio of all the formulations was in the range of 1.12 to 1.17 and all these values indicated that the precompression blends were showing good flow to excellent flow properties with low inter particle friction. Results are shown in **Table 2.**

Table 2: Flow properties of aceclofenac precompression blends (mean±s.d., n=3)

Formulation code	Bulk density (g/mL)	Tapped density (g/mL)	Carr's index (%)	Hausner's ratio	Angle of repose (º)
AH1	0.62±0.014	0.71±0.011	12.68	1.15	33.38±0.65
AH2	0.64±0.016	0.74±0.015	13.51	1.16	32.54±0.58
AH3	0.61±0.021	0.7±0.016	12.86	1.15	31.65±0.42
AH4	0.66±0.021	0.74±0.015	10.81	1.12	32.52±0.24
AH5	0.62±0.016	0.72±0.021	13.89	1.16	31.68±0.72
AT1	0.64±0.011	0.75±0.016	14.67	1.17	33.65 ±0.98
AT2	0.62 ±0.021	0.72 ±0.025	13.89	1.16	32.68 ±0.85
AT3	0.66 ±0.019	0.74 ±0.012	10.81	1.12	32.26 ±0.96
AT4	0.64 ±0.016	0.73 ±0.019	12.33	1.14	33.48 ±0.75
AT5	0.66 ±0.018	0.74 ±0.032	10.81	1.12	32.36 ±0.96

3.3. Evaluation of matrix tablets

The tablet properties of aceclofenac formulations are given in **Table 3**. The thickness of aceclofenac matrix tablets was in the range of 6.16-6.24 mm. The hardness of all the matrix tablets was in the range of 8-14 kp. The matrix tablets passed

the friability test as the % loss during the test was less than 1% confirming to the compendial limits. The tablets confirmed to the uniformity of weight test as the % deviation of weight was less than ±5%, complying with pharmacopeial specifications. The drug content of each individual preparation was found to be within the specified limits of 90 to 110% of the stated amount of aceclofenac.

Table 3: Evaluation of aceclofenac matrix tablets for initial screening

Formulation	Thickness[a] (mm)	Hardness[a] (kp)	Friability[b] (%)	Average weight of tablets[c] (mg)	Drug content[d] (%)
AH1	6.15±0.05	12±1.02	0.48	551.26±2.265	99.5±0.60
AH2	6.19±0.01	13±0.98	0.32	550.02±2.789	98.7±0.67
AH3	6.25±0.06	13±1.23	0.29	549.86±2.156	99.±0.97
AH4	6.29±0.07	13±1.25	0.25	552.02±2.568	101.2±1.54
AH5	6.34±0.04	13±0.98	0.19	549.86±2.985	100.1±0.40
AT1	6.14±0.07	12±1.58	0.46	552.02±2.325	101.7±0.86
AT2	6.19±0.02	13±1.59	0.35	549.56±2.265	102.3±0.38
AT3	6.24±0.06	13±1.52	0.29	548.65±1.856	99.8±0.31
AT4	6.30±0.01	13±1.31	0.19	550.06±1.856	100.2±0.49
AT5	6.34±0.03	13±1.12	0.15	550.98±2.582	101.3±0.55

a: mean±s.d., n=6; b: n=12 tablets (~ 6.6g); c: mean±% deviation, n=20; d: mean±s.d., n=3

3.4. *In vitro* dissolution studies

Among aceclofenac screening formulations, the composition AH5 (with HPMC) extended the drug release up to 27 hours whereas, the formulation AT5 (with tamarind gum) shown complete drug release within 24 hours.

Formulations with lower polymer concentrations (percentage of polymer to drug 10%, 45%) rapidly hydrated, resulting in weak matrix systems and could not extend the release beyond 4 to 6 hours. With further increase in polymer concentrations to 80, 115 and 150%, thicker gel formed inhibiting the dissolution media into matrix structure which could be due to closely packed swollen particles in thick gel and drug release was retarded significantly. The amount of polymer in the formulation was found to affect the drug release rate which could be due to the high viscosity of the gel layer around the drug in the tablet increases with increase in polymer concentration thus limiting the release of the drug.

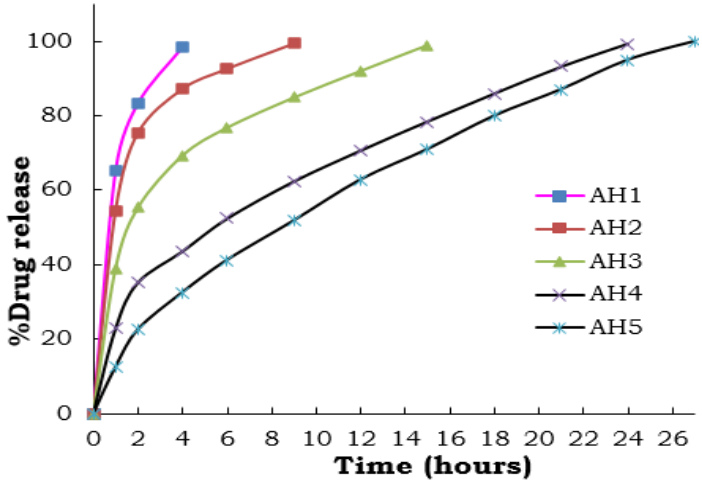

Figure 1: *In vitro* drug release profiles of aceclofenac-HPMC matrix tablets (AH1-AH5)

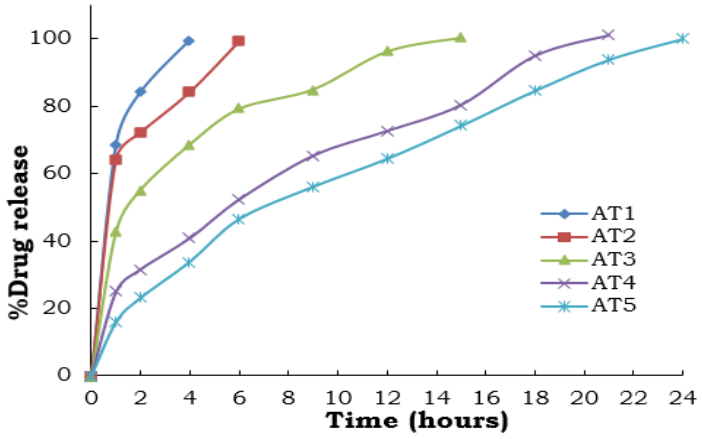

Figure 2: *In vitro* drug release profiles of aceclofenac-tamarind gum matrix tablets (AT1-AT5)

3.5. Evaluation of drug release kinetics and mechanisms

The order of release of all the formulations of aceclofenac matrix tablets were evaluated and compiled in **Table 4**.

Table 4: Correlation coefficient values (r) and release rate constants (k_0 and k_1) of aceclofenac matrix tablets

Formulation	Zero order		First order	
	r	k_0 (%hr^{-1})	r	k_1 (hr^{-1})
AH1	0.8707	22.1230	**0.9959**	0.4568
AH2	0.8069	8.8088	**0.9785**	0.2308
AH3	0.8608	5.0614	**0.9549**	0.1099
AH4	**0.9468**	3.4035	0.7677	0.1020
AH5	**0.9801**	3.4224	0.7632	0.0889
AT1	0.8604	22.1169	**0.9852**	0.5768
AT2	0.8416	13.3266	**0.9435**	0.3155
AT3	**0.8711**	5.2870	0.8671	0.2049
AT4	**0.9670**	4.1886	0.7897	0.1262
AT5	**0.9800**	3.8534	0.7721	0.1047

The correlation coefficient values indicated that all the formulations of aceclofenac of all the formulations followed first order release with lower polymer content (10% to 80%) and followed zero order with high polymer content (115% and 150%) in the tablet compositions.

The release mechanism was evaluated by using Higuchi, erosion and Korsmeyer-Peppas equation. The correlation coefficient (r) and Peppas exponent (n) values are shown in **Table 5**.

Table 4.19: Correlation coefficient values (r) and Peppas exponent values (n) of aceclofenac matrix tablets

Formulation	Higuchi	Erosion	Korsmeyer-Peppas
	r	r	n value
AH1	**0.9802**	0.7568	1.9677
AH2	**0.9468**	0.6470	1.2256
AH3	**0.9674**	0.6392	0.9541
AH4	**0.9951**	0.7089	0.8281
AH5	**0.9977**	0.7971	0.9060
AT1	**0.9758**	0.7512	1.9566
AT2	**0.9617**	0.6956	1.4721
AT3	**0.9730**	0.6503	0.9727
AT4	**0.9976**	0.7511	0.9204
AT5	**0.9970**	0.7959	0.9486

Correlation coefficient of Higuchi's plot of all formulations showed high linearity ranging from 0.9341-0.9990, indicating the drug release from matrix tablets involved diffusion, which means transport of drug from the matrix tablet into the dissolution media depending on the concentration. Further drug transport mechanism was assessed from Korsmeyer-Peppas plot and 'n' values were ranging from 0.8281-1.9459, indicating the drug transport mechanism follows either case II transport or super case II transport and drug release mechanism to be zero order release or relaxation/erosion mechanism. Aceclofenac matrix tablets prepared using semisynthetic polymer HPMC and natural polymer tamarind gum exhibited similar drug release parameters with both release order and release mechanisms, these polymers undergo diffusion in the aqueous medium due to solvent penetration effect, swelling, and polymer chain disentanglement and relaxation and these observations are in line with the reported literature.

4. CONCLUSION

The selected formulation ingredients showed no drug-excipient interaction. Wet granulation technique was used for preparation of matrix tablets of aceclofenac using PVP as binding agent. The granules prepared by wet granulation showed good to excellent flow properties. All the prepared matrix tablets exhibited acceptable official and other tablet properties indicating their quality. The drug release from the matrix tablets depended on the polymer concentration and increase in polymer concentration retarded the drug release effectively. HPMC polymer has shown better drug release control over the natural gum tamarind. However, the drug release was extended up to 24 hours with tamarind gum and the drug release followed zero order release kinetics with diffusion mechanism.

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