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Research Article

A NOVEL APPROACH IN DESIGNING ENTERIC-COATED ANTIPLATELET DRUG FOR BYPASSING STOMACH AND GASTRIC IRRITATION

SUGALI BANOOTH THIRUMALESH NAIK[1], MUNUSWAMY PURUSHOTHAMAN[2], KOTHAPALLI BANOOTH CHANDRA SEKHAR[3]

[1]Department of Pharmaceutics, Research Scholar, JNTUA, Ananthapuramu, Andhra Pradesh, India. [2]Department of Pharmaceutics, Scient Institute of Pharmacy, Hyderabad, Telangana, India. [3]Department of Chemistry, Krishna University, Machilipatnam, Andhra Pradesh, India. Email: thirunaikatp@gmail.com

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ABSTRACT

Objective: The innovative approach in this investigation is making an enteric-coated acetylsalicylic acid (ASA) for antiplatelet activity using a novel excipient.

Methods: A novel methodology used in making ASA tablets for tackling the stomach irritation of ASA, by including *Plantago ovata* seed mucilage as a tablet binder. ASA compatibility with *P. ovata* seed mucilage was judged by differential scanning calorimetry (DSC) and Fourier Transform Infrared (FTIR) studies. All tablets were prosecuted for flow properties, physicochemical constraints, and release.

Results: The enteric-coated tablets established no interface by FTIR and DSC lessons. All the tablets possessed physicochemical constraints. The ASA showed its opposition to discharge in the stomach (2 h) and errand in a basic buffer (within 45 min).

Conclusions: The work revealed that with the help of *P. ovata* as a tablet binder will resolve the disputes connected to gastric irritation.

Keywords: Antiplatelet, Mucilage, Binder, Tablet, Irritation.

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INTRODUCTION

The investigation was to make a postponed release stable tablet acetylsalicylic acid (ASA) to achieve bioavailability and to reduce the risk of gastric irritation. A low dose of ASA (75 mg) prescribed for its antiplatelet activity [1]; additionally, ASA is extremely moisture subtle. A day dose of ASA is proposed to discharge the drug after some adjournment or after passing the stomach.

Prolonged use of ASA causes ulceration in the stomach. Some attempts were made for the prevention of this issue by the coadministration of proton pump inhibitors (PPIs). However, they conclude with the interactions of ASA with PPIs [2,3]. Hence, it is essential to resolve such matters, the authors made a pioneering effort to include some excipient which should deserve both the purposes of gastro shielding actions and must help in the formulation. By performing an extensive literature survey, the authors found *Plantago ovata* seed mucilage, which has gastroprotective activity with tablet binding assets [4-6].

In this investigation, the author used *P. ovata* seed mucilage as a binder during tablet granulation and compressed them to tablets.

METHODS

Materials

The materials ASA was gifted from Waksman Selman pharmaceutical Pvt. Ltd, *P. ovata* seeds purchased from the local market of Anantapur. Lactose, MCC, Magnesium stearate, Talc, Ethylcellulose, HPMC Phthalate, Dichloromethane, Water (for HPLC), o-Phosphoric acid, and Acetonitrile were of Qualigens, Fine chemicals, Mumbai

The equipment and their make we as given below.

Electronic weighing balance (Citizen, CY-104, Mumbai); Wurster – Fluid bed coater (G.P.C.G.1.1); Bin blender (Tapasya); Tapped density tester (Electro lab); Hot Air oven (Shital Scientific Industries); Compression machine (Cadmach); Friabilator (Electro lab); Hardness tester-Pfizer (mLabs-SE-276; Digital pH meter (Inolab); Digital Vernier Calipers (Mitutoyo 500-196-20); Dissolution test apparatus (Lab India); UV-Visible double-beam Spectrophotometer (Shimadzu); Differential Scanning Calorimeter (Schimadzu-DSC-50); Fourier Transform Infrared (FTIR) (Perkin Elmer, spectrum-100); Stability chamber (Thermo lab); Microwave oven (CATA-2R); and Scanning Electron Microscope (JSM 6100 JEOL).

Methodology

Preformulation studies

FTIR spectral analysis

The toning among ASA with *P. ovata* was done by mixing 2 mg of ASA mixed with 200 mg of KBr, compacted to pellet, and screened (400–4000 cm^{-1}) with a resolution of 1 cm^{-1}.

DSC study

DSC thermograms of ASA with *P. ovata* were docked with diffraction scanning calorimeter, by heating 10°C/min with a range of 30–350°C.

Experimental methods

Isolation of P. ovata seeds mucilage

The isolation was performed as described by Abdul *et al.,* 2010 [7]. The *P. ovata* seeds were soaked in distilled water (~20 times) for 2 days, simmered for 10 min (for the liberation of mucilage). Later passed through a muslin cloth (marc detached), and the scum was collected. Acetone was included in an equal fraction (mucilage precipitates). Then, the mucilage was isolated and parched in an oven (<60°C), crumpled, sieved (# 80 mesh), weighed, and placed in a desiccator.

Characterization of P. ovata seeds mucilage

The extracted mucilage from the *P. ovata* seeds when assessed for their consistency, ash values, loss on drying, swelling index and pH, and flow properties (for dried powder). The physicochemical, phytochemical, and flow constraints of *P. ovata* seed mucilage [8,9].

Table 1: Composition of various ASA tablets

Ingredient	Formulation								
	AST-1	AST-2	AST-3	AST-4	AST-5	AST-6	AST-7	AST-8	AST-9
Aspirin	75	75	75	75	75	75	75	75	75
MCC	207	202	197	192	187	182	177	172	167
Lactose	10	10	10	10	10	10	10	10	10
Plantago ovata mucilage	5	10	15	20	25	30	35	40	45
Magnesium stearate	2	2	2	2	2	2	2	2	2
Talc	1	1	1	1	1	1	1	1	1
Weight of the tablet	300	300	300	300	300	300	300	300	300

ASA: Acetylsalicylic acid

Preparation of tablets

Preparation of ASA enteric-coated tablets
The enteric-coated tablets for delayed-release have these steps [10,11].

Preparation of core tablet
The ingredients (Table 1) screened (#40 mesh) and compressed to get ASA tablets.

Sub coating of ASA
The above tablets were water-proofed by sub coating (Tables 2).

Composition of enteric coat
The above-subcoated tablets were further coated with an enteric coating material (Table 3).

Evaluation of tablets

Pre-compression constraints

Bulk and tapped densities, Carr's index, Hausner's ratio, and angle of repose were judged for the tableting blend [7,12,13].

Post-compression constraints

The compressed tablets should possess good physicochemical constraints, as described below [14-16].

Weight variation
The weight of 20 tablets was individually weighed, and the mean was calculated and the deviation was calculated.

Diameter and thickness
Ten accidentally tablets from every batch were logged for diameter using a Vernier caliper, and the average was documented.

Hardness test
Each tablet was solely kept between the jaws Pfizer tablet hardness tester and pushed till it infatuates, and the mean was recorded.

As the ASA tablets were enteric-coated, no need to perform the friability test.

Disintegration test
ASA enteric-coated tablets were placed in 0.1M HCl (for 2 h), later in 6.8 pH, PBS for 30 min, and observed for tablet crumbling [17].

Uniformity of drug content
Ten tablets of ASA were weighed, triturated in a mortar. A ≡ 100 mg of ASA was relocated to a 50 ml volumetric flask, volume made to require with acetonitrile and formic acid (99:1), manually shaken, centrifuged at 3000 rpm for 5 min, and then diluted as essential. An aliquot of the diluted solution was introduced into a liquid chromatograph with a detector set at 230 nm. The rejoinders were associated with the standard to find the quantity in mg of ASA content in the sample. Table 4 depicts the chromatographic arrangements for ASA assessment [18].

***In vitro* dissolution studies**
The dissolution conditions for ASA, as explained (Table 5) [19].

Table 2: Sub coating for ASA tablets

Ingredient/tablet	Quantity
Ethylcellulose	2.5
Isopropyl alcohol	q.s
Dichloromethane	q.s

ASA: Acetylsalicylic acid

Table 3: Enteric coating for ASA tablets

Ingredient/tablet	Quantity
HPMC phthalate-55	1.40
Triethyl citrate	0.25
Talc	0.35
Dichloromethane	q.s
Methanol	q.s

ASA: Acetylsalicylic acid

RESULTS AND DISCUSSION

The physicochemical, phytochemical, and micromeritic constraints of *P. ovata* seed mucilage, as depicted in Table 6.

DSC studies
The thermogram of ASA showed an endothermic peak at 130.22°C, and it combined with excipient showed that a shift in thermogram was observed with a peak of 127.79°C (Fig. 1). These data confirm the impregnation of drugs with excipients used.

The FTIR spectra revealed that the characteristic peaks and stretches of ASA were found even in the blend, which indicate compatibility confirmations of ASA with excipients (Fig. 2).

The ASA blend showed an angle of repose, Carr's compressibility index, and Hausner ratio values <30°, 10%, and 1.25, respectively, which indicates the good flow properties (Table 7).

The tablets were subjected to uniformity of weight, hardness, thickness, and assay. The consequences of these censures unveiled nearly uniform thickness in all the formulations. The weights of all tablets were within the ±5% and passed the uniformity of weight as per official requests. All the tablets showed sufficient strength or hardness (>4 Kg/cm^2), representing physical strength for which required during handling and transport. The hardness is not an absolute gauge of strength. The enteric-coated ASA tablets did not show any sign of disintegration in 0.1 M HCl for 2 h and disintegrated within 45 min (2700 s) in pH 6.8 buffer, which verify the enteric coating efficiency of ASA enteric-coated tablets.

An appreciable uniformity in ASA content was observed among different batches of tablets, and the % of drug content was more than 95% (Table 8).

The enteric-coated ASA tablets were not shown any sign of dissolution in 0.1 M HCl for 2 h and >75% dissolved within 45 min in pH 6.8

buffer (Fig. 3), which reveals the firmness of the enteric coat on ASA tablets.

Table 4: The chromatographic conditions for the assessing ASA

Chromatographic conditions	Specification
Apparatus	HPLC
Column	C18, 250×4.6, 5 µ (Inertsil)
Wavelength (nm)	230
Detector	UV/PDA
Injection volume	20 µl
Flow rate	1.5 ml/min
Sample cooler temp	Ambient (25°C)
Run time	10 min
Elution	Isocratic

ASA: Acetylsalicylic acid

Table 5: Dissolution conditions fused in the study

Description	Condition
Apparatus	Dissolution apparatus USP type II (Paddle)
Medium	0.1N HCl for 2 h and then phosphate buffer (pH 6.8) for next 45 min
Medium volume	900 ml
Speed	100
Sampling intervals	30 min. 1 and 2 h (in 0.1 m HCl); 5, 10, 20, 30, 45, and 60 min (6.8 buffer)
Temperature	37±0.5°C

Table 6: Physicochemical, phytochemical, and micromeritic constraints of *Plantago ovata* seed mucilage

Parameter tested	Observation
Test	
Color	Pale yellow
Odor	Aromatic
Physicochemical evaluation	
Total ash	3.691±0.01% w/v
Water-soluble ash	1.525±0.01% w/v
Acid-insoluble ash	2.168±0.01% w/v
Ethanol-soluble extractive	4.058±0.02% w/v
Ether-soluble extractive	4.241±0.01% w/v
Loss on drying	2.028±0.02%
Swelling index	457.27±1.28
pH	7.6±0.1
Phytochemical evaluation	
Carbohydrate test (Molisch test)	A purple ring at the junction
Flow properties	
Angle of repose	25.26±0.11°
Bulk density	0.524±0.02
Tapped density	0.566±0.01
Carr's Index	7.092±0.03
Hausner's ratio	1.078±0.01

Values in mean±S.D; n=3

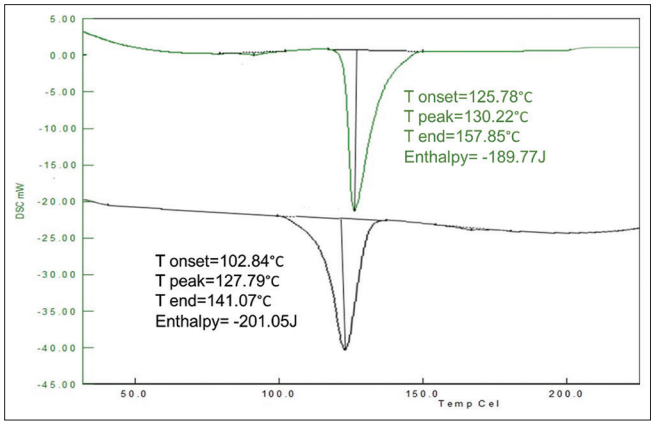

Fig. 1: Differential scanning calorimetry thermograms of acetylsalicylic acid and blend

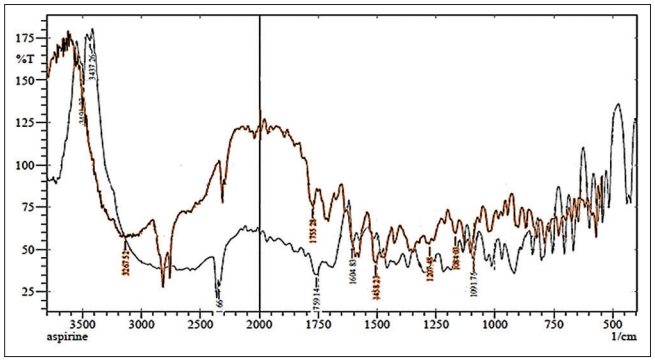

Fig. 2: Fourier transform infrared spectra of acetylsalicylic acid and its excipients

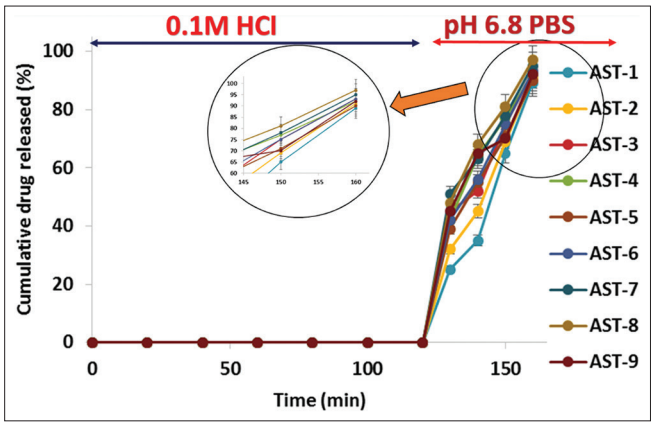

Fig. 3: Zero-order release plots for acetylsalicylic acid tablets

Table 7: Flow character specifications of ASA blend

Formulation	Flow properties				
	Angle of repose (°)	BD	TD	CI	HR
AST-1	28.98±0.05	0.528±0.01	0.548±0.01	3.649±0.02	1.037±0.02
AST-2	27.05±0.04	0.635±0.02	0.658±0.02	3.495±0.06	1.036±0.02
AST-3	26.41±0.02	0.519±0.01	0.534±0.02	2.808±0.05	1.028±0.03
AST-4	26.19±0.01	0.456±0.02	0.468±0.01	2.564±0.08	1.026±0.02
AST-5	29.36±0.02	0.625±0.01	0.644±0.01	2.950±0.07	1.030±0.01
AST-6	28.52±0.03	0.635±0.02	0.655±0.01	3.053±0.02	1.031±0.01
AST-7	26.39±0.02	0.546±0.01	0.569±0.02	4.042±0.05	1.042±0.05
AST-8	28.25±0.01	0.682±0.01	0.701±0.01	2.710±0.01	1.027±0.03
AST-9	27.15±0.02	0.567±0.01	0.589±0.01	3.735±0.06	1.038±0.02

Values in mean ±SD; trials (n=3). ASA: Acetylsalicylic acid

Table 8: Physical characteristics ASA tablets

Formulation	Physical parameter					
	Uniformity of weight (mg)	Hardness (cm^2)	Thickness (mm)	Disintegration (s)		Assay (%)
				0.1 M HCl (2 h)	pH 6.8	
AST-1	300.04±1.00	6.7±0.01	3.02±0.04	0.00	313±2	97.82±4.11
AST-2	301.20±1.60	5.5±0.01	3.01±0.03	0.00	332±4	99.83±8.95
AST-3	300.28±1.94	6.1±0.02	2.98±0.03	0.00	349±7	96.73±2.43
AST-4	301.98±2.01	6.6±0.02	3.00±0.03	0.00	378±4	97.06±4.65
AST-5	299.07±1.46	8.1±0.03	3.01±0.05	0.00	334±6	98.81±1.84
AST-6	302.50±1.68	7.8±0.02	3.01±0.01	0.00	318±4	98.48±2.05
AST-7	300.39±1.09	5.9±0.02	3.01±0.02	0.00	346±5	98.09±1.29
AST-8	299.32±2.07	6.4±0.05	2.99±0.04	0.00	394±4	98.46±2.04
AST-9	300.09±1.25	5.8±0.02	3.01±0.02	0.00	344±2	99.95±2.36

Values in mean ±SD; trials made (n=3). ASA: Acetylsalicylic acid

CONCLUSIONS

The distinct enteric-coated ASA was effectively made with the inclusion of *P. ovata* seed mucilage as a tablet binder. The prepared tablets were devoid of any ulceration of the stomach as *P. ovata* it already proved for its gastric protective actions.

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CONFLICTS OF INTERESTS

All the authors declare that they have no conflicting interests

AUTHORS' CONTRIBUTIONS

The authors announce together declares that all have contributed toward this research work. All the studies were conducted by all the authors together.

AUTHORS' FUNDING

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