

Monolithic floating tablets of Nimesulide

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Abstract

Floating Drug delivery system used to target drug release in the stomach or to the upper part of the intestine. The oral delivery of NSAID nimesulide was facilitated by preparing a non-disintegrating floating dosage form which can increase its absorption in the stomach by increasing the drug's gastric residence time. The polymer used were HPMC (low to high viscosity), guar gum, carbapol along with sodium bicarbonate as the gas-generating agents. The prepared tablets were evaluated their physicochemical properties and drug release. In-vitro release studies indicated that the nimesulide release from the floating dosage form was uniform and followed zero order release. The incorporation of guar gum helps to maintain the device's integrity and due to its viscosity property also affects the drug's release profile. Sodium bicarbonate which was used as the gas-generating agent causes the tablets to float for the required time >24hr.

Key words: floating drug delivery system, NSAIDS, nimesulide, HPMC.

INTRODUCTION

This novel NSAID is a relatively weak inhibitor of PG synthesis and there is some evidence to indicate relative COX-2 selectivity. Action may be exerted by other mechanisms as well, e.g. reduced generation of superoxide by neutrophil inhibition of PAF synthesis, TNF- α release, free radical scavenging inhibition of

metalloproteinase activity in cartilage, the analgesic, antipyretic and anti-inflammatory activity of Nimesulide has been rated comparable to other NSAIDs. It has been used primarily for short lasting pain anti-inflammatory conditions like sports injuries, sinusitis and other ear nose throat,

disorders, dental surgery, Bursitis, low backache, dysmenorrhea. Nimesulide is almost compatibly absorbed orally, 99% plasma protein bound, extensive value metabolized and excreted mainly in urine with $t_{1/2}$ 2-5hrs. Adverse effect of nimesulide are gastro intentional (epigastral heart burn, nausea, loose motion) dermatological (rash, pruritus) and central (somnolence, dizziness Gastric solubility of nimesulide is better, but a recent Italian study has shown that ulcer complication is as prevalent as with other NSAIDs.

MATERIAL

Nimesulide were obtained as a gift sample from Zim Laboratories pvt ltd. Nagpur, HPMC, sodium bicarbonate, talc from Loba Chemi pvt ltd. Mumbai and CMC were obtained from SD fine chem pvt ltd Mumbai. Magnesium stearate, talc, ethanol q.s, carbapol and all other chemicals are of analytical grade.

Formula

Ingredient	Quantity (mg)
Nimesulide	500
HPMC	1100
NaHCO ₃	41.5
CMC	512.5
Magnesium stearate	100
Talc	100
Carbapol	113.5
Ethanol	q.s.

PROCEDURE

Firstly all the ingredient were equally weighed. Then drug, HPMC, CMC, sodium bicarbonate were mixed in a pestle mortar. Then carbapol

dissolve in ethanol and mixed in above ingredient until the wet slug is formed of desired consistency. Then the slug is sieved through 22 mesh sieve so the wet granules were formed. The wet let granules were dried in hot air oven at 50 °C for 1 Hr. Then the dried granules were sieved through 16 mesh sieve. Then magnesium stearate and talc were added in to the granules. Dried granules were punched to form tablet using hand operated single punched.

EVALUATION

Buoyancy time

A tablet was introduced in to beaker containing 100ml of 0.1N HCL. The time taken by the tablet to come up to the surface and floated was taken as the buoyancy time. An average of three determination from which batch was taken for the floating forms

Dissolution studies

A USP XXII paddle type dissolution apparatus was used. 900ml of artificial gastric juice (without pepsin Ph 1.2) used as the dissolution media. One tablet was introduced in to the flask was rotated at 50rpm at a temp, of 37°C. Aliquot's 5ml were with down at predetermined time interval and the volume of the dissolution medium was kept constant. Throughout the dissolution run by replacing an equal vol, of the prewarm buffer by amount of the drug release was determined at 297nm. The residual drug remaining in thaw tablet an is was determined by homogenizing the tablet in 100ml of the buffer and estimating the

amount spectrophotometrically after proper dilution.

S.No	Model applied	R ² values
1.	Zero order release	0.9979
2.	First order release	0.9808
3.	Higuchi plot	0.9993
4.	Ritger and Peppas model	0.9813

RESULT AND DISCUSSION

The tablets prepared with HPMC showed maximum drug release but disintegrated within 4 Hrs while with the tablet prepared with HPMC, drug release was sustained significantly for 12Hr maintaining tablet integrity in the preliminary studies. It was observed that less than 50% of the drug was release form the non-floating dosage form prepared by the same method excluding the gas generating agents. From the R2 value of zero order release, first order release, Higuchi plot, Ritger and Peppas model it was found that drug release occur by means of diffusion controlled release.

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