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Preparation and Evaluation of Hydrodynamically Balanced Tablets Meloxicam

Ch. Ajay Babu*, M. Prasada Rao and B. Anusha
Dept.of Pharmaceutics, M.A.M College of Pharmacy, Kesanupalli, Narasaraopet, A.P, India

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***Corresponding Author Email:** ajay.babu2007@gmail.com

Abstract
In the present study Gastroretentive delivery systems of Meloxicam were successfully developed in the form of Hydrodynamically Balanced Tablets to improve the local action and ultimately its bioavailability. The tablets were formulated using different grades of polymers (HPMC K4M, HPMC K15M and carbopol) and effervescing agent (NaHCO3).IR spectra studies revealed that the drug and the polymers used were compatible. The evaluation parameters like hardness, friability and content uniformity were within the limits for various batches formulated. Buoyancy lag time, Total floating time, tablet density, Swelling studies showed satisfactory results for batch F1, F2, F3, F5, F6 and F8. The formulation F3 was evaluated for effect of hardness on floating lag time, and the results showed that the floating lag time increased as hardness increased due to reduction in porosity. *In vitro* dissolution of batch F3 containing HPMC K15M showed good drug release rate in comparison to remaining batches containing carbopol HPMC K4M, HPMC K10M which were not able to sustain their release up to 10 hrs. Formulations subjected to curve fitting analysis showed to best fit Korsemeyer-Peppas equation and followed non-Fickinian diffusion mechanism. Comparison study with marketed product Meloxicam ER showed that the optimized formulation F3 has better control over release rate in comparison with the marketed product. Hence it was concluded that formulation F3 containing HPMC K15M showed better controlled drug release rate in comparison to other polymers and showed that the release decreases as the viscosity of the polymer increases.

Keywords
Oral Drug Delivery, Gastroretentive DDS.

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INTRODUCTION
Oral drug delivery is the most widely utilized route of administration among all the routes that have been explored for systemic delivery of drugs via pharmaceutical products of different dosage form. Oral route is considered most natural, uncomplicated, convenient, and safe due to its ease of administration, patient compliance, and cost-effective manufacturing process.[1]

Pharmaceutical products designed for oral delivery are mainly immediate release type or conventional drug delivery systems, which are designed for immediate release of drug for rapid absorption. These immediate release dosage forms have some limitations such as. [2,3]

1) Drugs with short half-life requires frequent administration, which increases chances of missing dose leading to poor patient compliance
2) A typical peak-valley plasma concentration-time profile is obtained which makes attainment of steady state condition difficult.
3) The unavoidable fluctuations in the drug concentration may lead to under medication or overmedication as the values fall or rise beyond the therapeutic range.

4) The fluctuating drug levels may lead to precipitation of adverse effects especially of a drug with small therapeutic index, whenever over space medication occurs.

In order to overcome the drawbacks of conventional drug delivery systems, several technical advancements have led to the development of controlled drug delivery system that could revolutionize the method of medication and provide a number of therapeutic benefits.[4]

Oral controlled release drug delivery is a drug delivery system that provides the continuous oral delivery of drugs at predictable and reproducible kinetics for a predetermined period throughout the course of GI transit and also the system that target the delivery of a drug to a specific region within the GI tract for either a local or systemic action.

All the pharmaceutical products formulated for systemic delivery via the oral route of administration, irrespective of the mode of delivery (immediate, sustained or controlled release) and the design of dosage form (solid, dispersion or liquid), must be developed within the intrinsic characteristics of GI physiology. Therefore, the scientific framework required for the successful development of oral drug delivery systems consists of basic understanding of

(i) Physicochemical, pharmacokinetic and pharmacodynamic characteristics of the drug.
(ii) The anatomic and physiologic characteristics of the gastrointestinal tract and
(iii) Physicochemical characteristics and the drug delivery mode of the dosage form to be designed.

MATERIALS AND METHODS

Pre formulation Studies:

It is one of the important prerequisites in development of any drug delivery system. Pre formulation studies were performed on the drug, which included solubility, melting point, Flow properties and compatibility studies.

a) Solubility

Solubility of Meloxicam was determined in ethanol (95%), Chloroform, acetone, ether, and 0.1 N HCL. Solubility studies were performed by taking excess amount of Meloxicam in different beakers containing the solvent. The mixtures were shaken for 10 hrs at regular intervals. The solutions were filtered by using Whitman's filter paper grade no 41. The filtered solution were analysed spectrophotometrically.

b) Melting point

Melting point of the Meloxicam was determined by capillary method.

c) Flow properties

a) Angle of Repose (θ):

The frictional forces in loose powder or granules can be measured by angle of repose. This is the maximum angle possible between the surface of a pile of powder or granules and the horizontal plane.

The granules were allowed to flow through the funnel fixed to a stand at definite height (H). The angle of repose was then calculated by measuring the height and radius of the heap of granules formed.

$\tan\theta = h/r$

$\theta = \tan (h/r)$

where θ = angle of repose, h = height, r = radius

b) Compressibility Index:

The flowability of powder can be evaluated by comparing the bulk density (Do) and tapped density (Df) of powder and the rate at which it packed down. Compressibility index is calculated by –

$$\text{Compressibility index (\%)} = \frac{Df - Do}{Df} \times 100$$

Where

Do = Bulk density

Df = Tapped density

c) Compatibility Studies:

They provide framework for the drug in combination with the excipients in the fabrication of the dosage form and establish that active drug has not undergone degradation. This can be confirmed by carrying out infrared light absorption scanning spectroscopy.

I.R. Studies:

Infrared spectra of the physical mixture of the drug and the polymerswere prepared in the form of KBr pellets and subjected for scanning from 4000 to 400cm^{-1}using FT-IR spectrophotometer.

The application of infrared spectroscopy lies more in the qualitative identification of substances either in pure form or in the mixtures and as a tool in establishment of the structure.

Since I.R. is related to covalent bonds, the spectra can provide detailed information about the structure of molecular compounds. In order to establish this point, comparisons were made between the spectrum of the substance and the pure compound.

Formulation of Hydro Dynamically Balanced Tablets:

Floating matrix tablets containing Meloxicam were prepared by direct compression technique using varying concentrations of different grades of polymers with sodium bicarbonate.

All the ingredients except magnesium stearate were blended in glass mortar uniformly. After sufficient mixing of drug as well as other components, magnesium stearate was added and further mixed

for additional 2-3 minutes. The tablets were compressed with 13mm punch using hydraulic press. The weight of the tablets was kept constant for formulations F1 to F10. The composition of all formulations was given in Table 1.

Evaluation of powder

a) Angle of Repose (θ):

The frictional forces in a loose powder or granules can be measured by angle of repose. This is the maximum angle possible between the surface of a pile of powder or granules and the horizontal plane. The granules were allowed to flow through the funnel fixed to a stand at definite height (H). The angle of repose was then calculated by measuring the height and radius of the heap of granules formed.

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Where Do = Bulk density, Df = Tapped density

Evaluation of tablet

a) Shape of Tablet:

Directly compressed tablets were examined under the magnifying lens for the shape of the tablet.

b) Tablet Dimensions:[71]

Thickness and diameter were measured using a calibrated dial caliper. Three tablets of each formulations were picked randomly and thickness was measured individually.

C) Thickness:

The dimensions of the tablet like thickness, length was measured using vernier-calipers. Ten tablets were selected randomly for this test and the average value was reported.

d) Hardness:[71]

Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. The hardness of the tablets was determined using Monsanto hardness tester. It is expressed in kg/cm2. Three tablets were randomly picked and hardness of the same tablets from each tablet was determined.

RESULTS AND DISCUSSION

Tablet Density, Buoyancy Lag Time, Total Floating Time

Batch	Tablet density	Buoyancy lag time (sec)	Total floating time(Hrs)
F1	0.93	62	>12
F2	0.88	54	>12
F3	0.82	49	>12
F4	0.99	134	>6
F5	0.85	58	>12
F6	0.89	55	>12
F7	0.95	125	>7
F8	0.86	118	>12
F9	0.93	107	>9
F10	0.90	102	>10

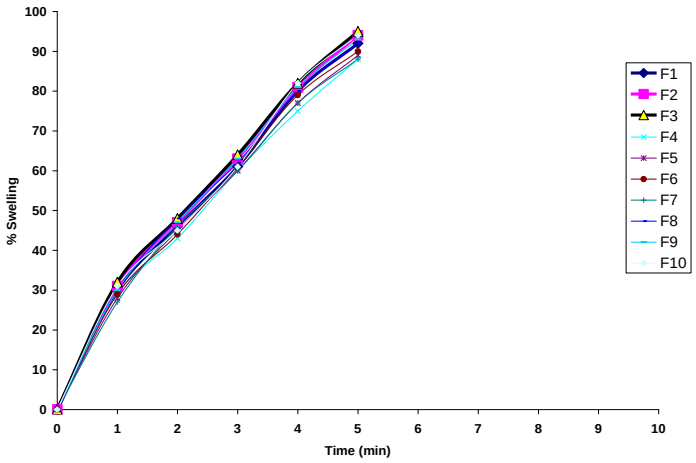
Tablet density: To provide good floating behavior in the stomach, the density of the device should be less than that of the gastric contents (1.004g/cm3). All the batches showed density below than that of gastric fluid (1.004). The values are shown in Table 1

Buoyancy Study: Formulation F3 containing HPMC K15M showed good BLT of 49 sec, while the formulation containing chitosan alone and in combination with HPMC K15M showed highest BLT, and TFT of less than 12 hrs. This may be due to the amount of polymer and gas generating agent, which were kept constant in the present study. The gas generated cannot be entrapped inside the gelatinous layer, and it escapes leading to variation in BLT and TFT.

Swelling factor: - In the present study, the higher swelling index was found for tablets of batch F3 containing HPMC K15M having nominal viscosity of 15,000 cps. Thus, the viscosity of the polymer had major influence on swelling process, matrix integrity, as well as floating capability, hence from the above results it can be concluded that linear relationship exists between swelling process and viscosity of polymer.

Swelling Index of Tablets of Batch F1 to F10

Time in Hrs	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
1	30	31	32	29	28	29	27	30	30	31
2	46	47	48	43	45	44	46	48	47	45
3	61	63	64	60	60	61	60	62	63	61
4	80	81	82	75	77	79	77	80	81	82
5	92	94	95	88	89	90	88	92	93	94



Swelling Index

CONCLUSION

In the present study Gastroretentive delivery systems of Meloxicam were successfully developed in the form of Hydrodynamically Balanced Tablets to improve the local action and ultimately its bioavailability. Buoyancy lag time, Total floating time, tablet density, Swelling studies showed satisfactory results for batch F1, F2, F3, F5, F6 and F8. The formulation F3 was evaluated for effect of hardness on floating lag time, and the results showed that the floating lag time increased as hardness increased due to reduction in porosity.

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