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Original Article

Formulation and Evaluation of Paracetamol Matrix Tablet Using Natural Polymer

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ABSTRACT

Matrix tablets of Paracetamol were prepared utilizing natural polymer chitosan. The tablets represented sustained drug release which is required for the drugs like Paracetamol with low bioavailability and low half life. The tablets can sustain the drug release which can overcome such problems. Moreover the tablets contain chitosan which also is a permeability enhancer and hence could be utilized to increase the permeability of the drugs like Paracetamol with very low permeability. The tablets possess high potential for being developed as sustained release dosage forms for drugs with low permeability , bioavailability and lower half life.

Keywords: Matrix tablets, Paracetamol, natural polymer, chitosan, bioavailability

INTRODUCTION

Oral route is one of the most popular routes of drug delivery due to its ease of administration, patient compliance, least sterility constraints and flexible design of dosage form (Indian Pharmacopoeia).

Tablets: Over 90% of the formulations manufactured today are ingested orally. This shows that this class of formulation in the most popular worldwide and the major attention of the researcher is toward this direction. With advanced in technology and increase in awareness, toward modification in standard tablets is done to achieve better acceptability as well as bioavailability because of which newer and more efficient tablet dosage forms are being developed. The main reasons behind formulation of different type of the tablets are to create a delivery system that is relatively simple and in expensive to manufacture, provide the dosage form that is convenient from patients perspective and utilize an approach that is unlikely to add complexity during regulatory approval process. To understand each dosage form, tablets here are classified by their route of adrninistration and by the type of drug delivery system they represent within route.

Overview on types and class of tablets:

A. Tablet lngested Orally:

These tablets are meant to be swallowed intact along with sufficient quantity of the potable water. Exception are chewable tablet and oral dispersible tablets. Standard compressed tablets this class includes tablets like, multiple compressed tablets, compression coated tablets, layered tablets, modified released tablets etc.

B. Tablets used in the oral cavity:

The tablets under this group are airned to released active pharmaceutical ingredient in the oral cavity or to provide local action in this region. The tablets under this category avoids first-pass metabolism, decomposition in gastric environrnent, nauseatic sensations and gives rapid onset of action. The tablets fommlated for this region are designed to fit in proper region of oral cavity. This class includes tablets like lozenges and troches, sublingual tablets, buccal tablets, dental eones, oral dispersible tablet etc.

C. Tablets administered by other routes:

These tablets are administered by other route except for the oral cavity and so the drugs are avoided from passing through gastrointestinal tract. These tablets

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may be inserted into other body cavities or directly placed below the skin to the absorb into systemic circulation from the site of application. This class include tablets vaginal tablets, implants etc.

D. Tablets used to prepare solution:

The tablets under this category are required to be dissolved first in water or other solvent before administration or application. This solution may be for ingestion or parenteral application or for topical use depending upon type of medicament used. This class includes tablets like effervescent tablet, hypodermic tablet etc.

Matrix Tablets:

Definition:

Matrix tablets are the type of tablet which is designed such that it releases it contents regarding first order kineticks or zero order kinetics due to special arrangement and combination of hydrophobic and hydrophilic polymers as an excipient to form a matrix. example of such a matrix tablets are, controlled release tablet, sustained released tablet. these all come under the category of modified release tablet.

MATERIAL AND METHOD:

Preformulation study: Pre-formulation may be described as a phase the research and development process where the formulation scientist characterizes the physical, chemical and mechanical properties of new drug substances, in order to develop stable, safe and effective dosage forms. Ideally the pre-formulation phase begins early in the discovery process such that the appropriate physical and chemical data is available to aid the selection of the new chemical entities that enter the development process. During this evaluation, possible interactions with various inert ingredients intended for use in final dosage form is also considered in the present study. The following data must be considered.

Table 1: Preliminary screening of formulation of sustained release layer of paracetamol using natural, hydrophillic and hydrophobic polymers

lngredients(mg)	SRl	SR2	SR3	SR4	SRS
Paracetamol	50	50	50	50	50
HPMC 15cps	35	55	75	-	-
Na- CMC	70	50	30	25	30
Gar Gum	-	-	-	45	40
Mg- Stearate	3.5	3.5	3.5	3.5	3.5
Lactose	188	188	188	223	223
Tale	3.5	35	35	35	3.5
Total	350	350	350	350	350

Organoleptic property:

Table no 2.: Description of the drug (Paracetamol).

S NO.	Description	Paracetamol drug
1	State	Solid
2	Colour	White or yeUowish
3	Odour	Odourless
4	Texture	Amorphous powder

Solubility studies:

An excess quantity of Paracetamol was taken separately and add in 1O ml of different solutions. These solutions were shaken well for few minutes. Then the solubility was observed and observations are shown in the table no.3.2-

Table no 3: Solubility studies of drug in different solvents.

Solvents	Solubility of Paracetamol

Water	Freely soluble
Methanol	Soluble
Acetone	Insoluble
Alcohol	Sparingly soluble
Methylene chloride	Practically insoluble

Partition coefficient:

It is a measurement of drug's hydrophilicity and an indication of its ability to cross cell membranes, partition coefficient of Paracetamol was found out by suspending known amount of drug in 1:1 mixture of octanol/water. The concentration of the drug in oil and water was determined through the absorbance of the dilution of the drug

Table no 4 Partition coefficient of drug

Drug	Specification (Log P value)	Observation (Log P value)
Paracetamol	-8.08	-7.98

Loss on drying studies:

About 1g of the powder was weighted and kept for checking the loss on drying on a moisture sensitive balance at 105°C for 3 minute % loss of moisture was 8%.

pH of the solution:

The pH study was done for the drug by dissolving it in their water as solvent and determining the pH while the help of pH meter. The pH value of clrug has been shown in tableno.3.4.

Table no. 5 pH of drug solution

Drug	Specification	Observation
Paracetamol	5.5-7.5	6.8

Melting point:

Melting point of the clrug was determined by the Theil 's Apparatus. It can be performed by filling of the drug in capillary tube and tied this capillary tube at the bottom of thermometer with the help of thread. Now filled Theil's with light liquid paraffin and holded this tube with the help of burette stand than place burner at the bottom of tube, dip the thermometer in this liquid paraffin and the note the point which drug started melting in the capillary. Melting point of drug has been shown in the table no 3.3.

Table no 6 Melting point of drug

Drug	Specification	Observation
Paracetamol	I 46-I48°C	I47- I49°C

Standard calibration curve for Paracetamol:

Preparation of standard solution:

For preparation of standard solution, I Omg of drug was dissolved in IO ml of distilled water (upto IO ml). This is stock solution.

Preparation of sample:

Prepared O.O IN KMn04 solution and O. IN NaOH solution and mixed 5ml of KMn04 of the solution in 5ml of NaOH solution. Withdrawn O.I, 0.2,0.3,0.4,0.5 ml from stock solution and added 5ml of mixture of KMn04 in NaOH solution and up to volume upto I Oml with the help of distilled water. Drug solution was scanned on UV Visible spectrophotometer to obtain A.max of the drug which was found to be 6IO nm. Absorbance of different

aliquots was measured at the A.max specific for that drug on UV Visible spectrophotometer (Model: UV - 1700 Shimadzu, Japan) at 6I Onm. Linear regressed calibration curve was constructed which has been represented in graph given table no 3.6.

Table no 7: Absorbance of different aliquots of Paracetamol at 610 nm

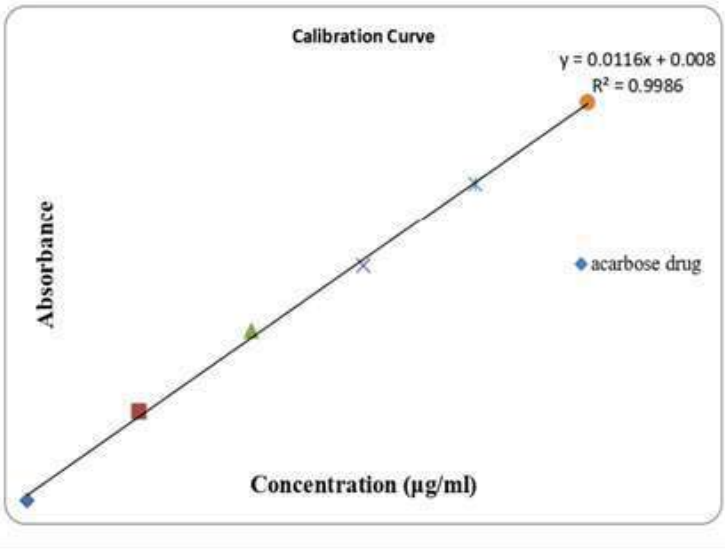

Figure no.3.1: Graph showing linearly regressed calibration curve of Paracetamol

Drug-Excipient compatibility studies:

The pure drug and along with formulation excipients were subjected to compatibility studies and studies were carried out by mixing definite proportion of drug and excipients and kept in glass vials which were stored at 40ºC±2ºc and 75±5%RH for one month. Drug- Excipient compatibility studies have been shown in table no 5.7.

RESULT AND DISCUSSION

In the matrix tablet, HPMC and chitosan were used as retardant materials for sustained release action. Preformulation of the drug was carried out with respect to different parameters. Drug was separately tested for their physicochemical characteristics. Melting point of Paracetamol was found to be l46-l48°C respectively. Similarly, solubility studies were conducted for the drug in different solvents. It was found that the drug was freely soluble in water, soluble in methanol, insoluble in acetone, sparingly soluble in alcohol and practically insoluble in methylene chloride. Partition coefficient of the drug was calculated which was found to be - 7.09 of Paracetamol. The pH of the drug solution was found to be 6.8. UV spectroscopy of the drug was also performed and the drug was scanned on different wavelengths. Ainax of Paracetamol was found to be 6lünm. All the values calculated were found to be concordant which that of the standard values reported in Standard Pharmacopoeial books. IR spectroscopy study was performed for the drug, the IR spectrograph for the drug was found to be in agreement with that of the standard IR graph reported. Compatibility studies was performed by keeping the drug mixed with that of the different excipients which was kept for one month and no change was observed with respect to physical properties of the drug which represents that the excipients are compatible with that of the drug. Itwas observed that there was no significant shift in the melting point of the drug when taken alone or in combination with that of polymer used. On the basis of the compatibility studies, it was found that drug is compatible with all other excipients selected for the study and hence can be used in combination for the preparation of the tablets. Paracetamol sustained release matrix tables were prepared by wet granulation method, different formula were designed to formulate the tablets which have been mentioned in table no.9. Inthe matrix tablet, HPMC were selected as retardants material for the sustained released action (more than 20% drug released in 1hrs). MCC was selected as a binder with 8%. Lactose and Dicalcium phosphate was selected as a diluents with 17.6% and

Magnesium stearate was selected as a lubrication and Tale was selected as a glident. All different formulation containing different amount of HPMC, Lactose and Dicalciumphosphate were prepared to formulate the tablets. Angle ofrepose was found to be between 28.2°- 35.24°, where sorne of the blend fell between the specified limit of 20° - 30° representing good flow. Bulk density was found to be between 0.52 - 0.64 g/ml. Tapped density was found to be between 0.60 - 0.76 g/ml. Carr's index (%) was found to be in the range of 11.66 - 16.66, all the powder blend are well within the specification limit. Hausner's ratio was found to be between 1.13 -1.2. With this the powder blends were found to be free flowing material and showed suitability to be compressed as tablets of expected weight. It was observed that hardness of the all sustained released tablets were measured by Monsanto hardness tester and were controlled between 5 to 6 kg/cm2. The thickness of all SR matrix tablets was measured by vernier caliper and was ranged between 2.44-2.56. The loss in total weight of the tablets due to friability was less than 0.5%, the high value of crushing strength and low friability indicated that the compressibility of Paracetamol and adjuvant was good. The swelling index was calculated with respect to the time. It was observed that as time increases, the swelling index was increased proportionally with the rate of hydration up to 3 hrs. On the basis of the parameters viz. weight variation, hardness and friability the best formula was selected. F-2 formulation was found to be the best formula and hence was taken as the optimized formula. Tablets prepared out of formula F-2 represented a weight variation of 2.22±0.11, hardness of 5.3±0.32, friability of 0.28±0.01, swelling index of 52±0.96 and disintegration time of 5.30±0.11. The tablets prepares from lactose as an excipient acquired a sticky nature and hence were not taken for consideration for further study. The tablets prepared out of the optimized formula was taken into consideration for further in vitro dissolution drug release study. In- vitro dissolution studies of the sustained release matrix tablets of Paracetamol were performed using USP type II dissolution apparatus (paddle) at 50 rpm. The study was performed for 12 hours, and percentage drug release was calculated at 1 hours' time intervals. The drug release profile were characterized by an initial burst effect (more than 18% drug release in 1 hrs) followed by a sustained release thereafter. The formulation F-2 contained chitosan which might have sustained the release since it is also known for its polymeric sustaining effect. The formulation F-2 gave 89.57±0.24% of the drug release in 12 hrs of study. This is in fact true for the polymeric tablets since the surface drug gives a burst effect thereby releasing a amount of drug at once and since polymer like chitosan and HPMC are present which provide matrixing to the tablet, the further release is sustained. The drug release also resembles a higuchi pattem which indicates sustained drug release from the matrix tablets. This is again due to the presence of the polymer like chitosan and HPMC.

SUMMARY & CONCLUSION

Matrix tablets of Paracetamol were prepared utilizing natural polymer chitosan. The tablets represented sustained drug release which is required for the drugs like Paracetamol with low bioavailability and low half-life. The tablets can sustain the drug release which can overcome such problems. Moreover, the tablets contain chitosan which also is a permeability enhancer and hence could be utilized to increase the permeability of the drugs like Paracetamol with very low permeability. The tablets possess high potential for being developed as sustained release dosage forms for drugs with low permeability, bioavailability and lower half life

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