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COMPARATIVE STUDY ON EFFECT OF HERBAL DILUENTS ON RELEASE OF DRUG

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ABSTRACT

The main objective of this research was to introduce and evaluate disintegrant property of natural excipients like Potato starch and Maize starch in tablet formulation. Pharmaceutical excipients developed from natural sources are economic. Potato starch and Maize starch were prepared and physicochemical properties like solubility, iodine test, angle of repose, bulk density, tapped density, carr's index, hausner's ratio and melting point were evaluated. The interaction between the excipcents and Paracetamol was also studied through FTIR spectroscopy. Tablets were then prepared by direct compression method using different disintegrants and the disintegration time of the tablets formulated was determined. Dissolution study was conducted to characterize release mechanism from the tablet system and data were fitted to various kinetic models. It was found that tablets with potato starch and maize starch disintegrate more rapidly than the tablets with microcrystalline cellulose. The prepared formulations were passed the evaluation test that is weight variation, hardness, friability and content uniformity. The mechanism of drug release from tablets was found to be non-Fickian, anomalous transport. Results from various evaluations suggested that potato starch and maize starch could be used as disintegrants in tablet formulation.

KEYWORDS: Potato starch, Maize starch, Natural excipients, Disintegrant, Paracetamol.

INTRODUCTION

Researchers are being carried out to reduce the patient compliance and for an effective therapy. The most widely utilized route of administration is oral drug delivery among all the routes that have been explored for the systemic delivery of drugs. Appropriate design and formulation of a dosage form need consideration in the physical, chemical and biologic

characteristics of the drug substances. Excipients help the formulation design and perform a wide range of functions to obtain desired properties in the finished drug product. Excipients are the additives used to convert pharmacologically active compounds in to pharmaceutical dosage forms suitable for administration to patients. Present day researcher are looking for natural excipients as they believe that anything natural will be more safe and devoid of side effects. Advantage of natural excipients are low cost and natural origin free from side effects, biocompatibility & bioacceptance, renewable source, environment friendly processing, local availability, better patient tolerance as well as public acceptance, they comprise the natural economy by providing inexpensive formulation to people.[1]

In the present context the focus was the study of natural excipients. For most tablets, the first important step is break down of tablets in to smaller particles or granules, a process is known as disintegration. Disintegration test is provided to determine whether tablet disintegrate within the prescribed time when placed in liquid medium as specific experimental condition.[2] Starches are used extensively in pharmaceutical industries as disintegrants, binders and lubricants in tablet formulation. Starches are believed to extent its disintegrating property by absorption of moisture and swelling of the grain followed by rapture of tablet core.

MATERIALS AND METHOD

Materials

Paracetamol was received as a gift sample from Macsur Pharma India Pvt Ltd, Puducherry, India. Lactose (Spectrum reagent & chemicals Pvt.Ltd), Microcrystalline cellulose (Chemdyes co, Rajkot), Acacia (Nice chemicals Pvt.Ltd), Talc (Spectrum reagent & chemicals Pvt.Ltd), Magnesium stearate (Otto chemicals, Mumbai), Potato starch & Maize starch extracted were used as tablet excipients.

Methods

Extraction of Potato Starch

Potato was thoroughly washed and all foreign materials were removed. The potato was peeled, weighed and washed. The washed potato was pulverized using a blender. Enough quantity of water was added to the pulp which then passed through a sieve. The filtrate was allowed to settle and 0.1 N sodium hydroxide was added to separate the starch and proteinous materials as well as to neutralize the prevailing slight acidity. Excess sodium hydroxide was removed by washing several times with distilled water. The clear supernatant fluid was

poured away while sediment starch was collected on a tray and air-dried on a table at room temperature.[3]

Extraction of maize starch

First of all the maize grain is softened by soaking it in an aqueous solution of sulphuric acid (0.2%) at 50^0C for about 2 to 3 days.

In this way the disintegration takes place and the embryo or grains are readily librated and permitting the separation of starch from fibres.

The softened grain is crushed between rollers, which partially crush the grains, and liberate most of the starch from the embryo or grains, then water is added and milky liquid is filtered through sieves. In this way the cell debris and glutens are separated through starch, as starch is heavier than glutin.[3]

Characterization of Potato starch and Maize starch (Pre-evalution parameter)[4]

Solubility Test

The solubility of the Maize starch and Potato starch in cold water was determined and the results recorded.

Iodine Test

1g of Maize starch and Potato starch was boiled with 15mls of water. After cooling to 1ml of the mucilage, 2 drops of 0.1N iodine [tri-iodide anion ($I3^-$)], solution was added and Starch turns into an intense "blue-black" colour.

Angle of repose

A 30 g sample was poured into a plugged glass funnel with the tip, 10 cm above the flat surface of the bench. The granules were allowed to flow freely through the orifice of the funnel to form a heap whose height and diameter were determined.

The angle of repose was calculated using the equation below:

$$\tan \theta = h/r$$ (Where h = height and r = radius of circular heap)

Bulk Density

A 30g weight of each of the maize starch and potato starch to be used as carrier was weighted and poured in to a 100ml measuring cylinder and the volume was recorded. The bulk density was then calculated.

Bulk Density (BD) = M / V (Where M is mass and V is volume)

Tapped Density

A 30g weight of each of the maize starch and potato starch was weighted and poured into a 100ml measuring cylinder and tapped on a hard surface 30 times from about 2cm height and the volume was recorded.

Tapped Density (TD) = M / V (Where M is mass and V is volume)

Carr's Index

Carr's Index (%) was determined using the following relationship

C.I. = (TD – BD/ TD) x 100

Hausner's ratio (H.R)

Hausner's ratio was determined using the following relationship

H.R=TD/BD (Where TD is Tapped density, BD is Bulk density)

Swelling capacity

The tapped volume occupied by 10g of each Maize starch and potato starch (*Vd)* in a 100ml measuring cylinder was noted. The powder was then dispersed in 85ml of distilled water and the volume made up to 100ml with more water. After 18hours of standing, the volume of the sediment, (*Vw)* was estimated and the swelling capacity was computed.

Compatibility study

Before formulation of a drug substance into a dosage form, it is essential that it should be chemically and physically characterized. Compatibility studies give the information needed to define the nature of the drug substances and provide a frame work for the drug combination with pharmaceutical excipients in the fabrication of a dosage form. One of the requirements for the selection of suitable excipients or carrier for pharmaceutical formulation is its compatibility. Therefore in the present work, a study was carried out by using Shimadzu FTIR spectrometer to find out if there is any possible chemical interaction between Paracetamol and excipients respectively. The samples were powdered and intimately mixed

with dry powdered potassium bromide. The powdered mixture was taken in a diffuse reflectance sampler and the spectra recorded by scanning in the particular wavelength region (1650 cm-1) using Shimadzu FTIR spectrometer. The IR spectrum of drug was compare with that of the physical mixture of the drug and excipients used to check for any possible drug-excipients interaction.

Formulation of Tablet

Four different batches of tablets each containing 500mg of Paracetamol were formulated and evaluated. In all four bathes the tablets were formulated employing Paracetamol alone and Starch (20%) as diluents and direct compression method. In all the bathes acacia (20%) as binder, talc (5%) and magnesium stearate (5%) as lubricants were used. In formulation F1 Potato starch (20%), F2 Maize starch (20%), F3 Potato starch(10%) and Maize starch (10%) and F4 Microcrystalline cellulose [MCC] (20%) as Diluents(Pharmaceutical) were used. In each batch 50 tablets were prepared.[5]

Table 1: Composition of Different Batches of Paracetamol Tablet.

Ingredients Mg/Tablet	Formulations			
	F1	F2	F3	F4
Paracetamol	250	250	250	250
Potato starch	100	-	50	-
Maize starch	-	100	50	-
Microcrystalline cellulose	-	-	-	100
Acacia	100	100	100	100
Talc	25	25	25	25
Magnesium stearate	25	25	25	25
Total wt of the tablet (mg)	500	500	500	500

Evaluation of Tablets[6]

Weight Variation

The USP weight variation test was performed by taking 20 tablets from a batch. Then 20 tablet, were weighed and the average weight was taken. Then each tablet was weighed individually. The percentage deviation can be determined by using the following formula.

$$\% \text{ Deviation} = \frac{\text{Average weight (mg)-Individual weight Average (mg)} \times 100}{\text{Average weight (mg)}}$$

Hardness Test

Pfizer hardness tester was used for measuring the hardness of the formulated Paracetamol tablets. From each batch five tablets were taken at random and subjected to test. The mean of these five tablets were given in the table.

Friability

It is a measure of tablet strength. The friability was determined by using Roche Friabilator. 10 tablets were taken and their weight determined. Then they were placed in the friabilator and allowed to make 100 revolutions at 25rpm. The tablets were then dusted and reweighed. The percentage weight loss was calculated by using the following formula.

$$F=100\times(1-w/wo)$$

Where, *wo* = Weight of tablets before friability

w = Weight of tablets after friability

Drug content Uniformity

Drug content uniformity is carried out by performing assay of paracetamol tablet as per IP, USP. The absorbance was measure at 257nm in a UV spectrophotometer with suitable dilution.

Disintegration Test

To meet the USP standard all particles of tablet must pass through 10 mesh screen in the time specified.

Dissolution Test

Dissolution was carried out using USP dissolution apparatus II (paddle apparatus). Dissolution of tablets was carried out in 900ml-dissolution medium. The dissolution medium for Paracetamol tablet was pH 1.2. The temperature of dissolution medium was maintained at 37ºC ± 2ºC. The agitation intensity was 100rpm. The samples of dissolution medium were withdrawn through a filter at different time intervals. Equal volume of fresh medium having same temperature was replaced at each time. The samples were suitably diluted and the amount of active ingredient was determined spectrophotometer with respect to the reported methods.

Dissolution Kinetics

To study the release kinetics, data obtained from *in vitro* drug release studies were plotted in various kinetic models: Zero order (cumulative amount of drug released vs time), First order (log cumulative percentage of drug remaining vs time), Higuchi's model (cumulative percentage of drug released vs square root of time), Hixon-Crowell (cube root of amount remained to be absorbed vs time) and Korsmeyer's (log cumulative percentage of drug released vs. log time).

RESULTS AND DISCUSSION

Compatibility study

FTIR spectroscopy was performed to assess the compatibility of Paracetamol with excipients. Analysis of Paracetamol structure reveals that few intense peaks which are characteristic (1650, 1750, 1850, 1890, 1920, and 2016.16) of the drug, the similar peaks were observed in all formulations. The results clearly indicate no shifting of peaks was significantly found, indicating the stability of the drug during tablet formulation. Thus the IR study indicates stable nature of Paracetamol in the tablet formulations. This also confirmed that the drug and polymer does not interact.

Table 2: Result of Physicochemical properties of starch powder.

Properties	Potato starch	Maize starch
Solubility	Insoluble	Insoluble
Iodine Test	Positive	Positive
Angle of Repose(Ɵ)	24.22±0.12	37.59±0.25
Bulk density(g/ml)	0.5±0.1	0.75±0.12
Tapped density(g/ml)	0.83±0.12	0.66±0.1`
Carr's Index (%)	9.63±0.22	24.24±0.20
Hausner's Ratio	1.10±0.16	1.32±0.12
Swelling Capacity	0.153%	0.411%
Melting point (^{0}C)	70	256

Maize starch is Insoluble in water where Potato starch is practically insoluble in water. The powders also turn blue black on addition of iodine solution which confirmed the presence of starch. An angle of repose 24.22 and 37.59 were obtained for potato starch and maize starch respectively which all fall with the required range for pharmaceutical powders which is 25-45, that of the Maize starch which is Moderate flow and potato starch which is excellent and indicates a better flow property. Angle of repose has been used to characterize the flow properties of powders, it also related to inter particulate friction or resistance to movement between particles. The Carr's index of the potato starch is 9.63% and indicates excellent flow

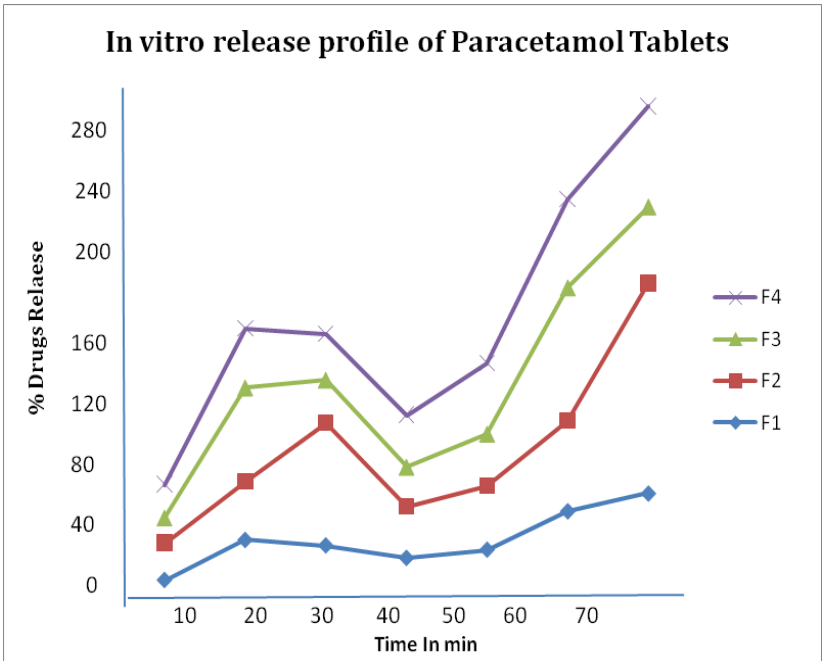
ability where maize starch is 24.24 and its indicates flow ability. The housner's ratio of potato starch is 1.10 which indicates Excellent where maize stach is 1.32 indicates the fair passable flow ability.

Table 3: Result of Physical evaluation of tablets.

Formulations	Hardness (kg/cm^2)	Average weight variation (%)	Friability (%)	Drugs content(mg)	Disintegration time (sec)
F1	4.8±0.12	2.17±0.13	0.58	98.20	150
F2	5.1±0.14	4.25±0.10	0.71	97.50	170
F3	4.6±0.12	3.06±0.25	0.66	95.50	165
F4	5.0±0.20	2.00±0.35	0.54	99.21	198

The hardness values ranged from 4.6 to 5.1 kg/cm^2 for all formulations. The entire tablets passes weight variation test as the average % weight variation was the pharmacopoeial limit of 5%. The friability values were found to be within the limit ranged from 0.54 to 0.71%. The drug content of Paracetamol determined at 287nm ranges from 95.50 to 99.21 and complies with IP standard. In the study, potato starch and maize starch was employed as disintegrant and its effect was compared with microcrystalline cellulose. Tablets produce from the potato starch and maize starch show a relative lower disintegration time compared to that of the microcrystalline cellulose.

The dissolution process of a tablet depends upon the wetting followed by disintegration of the tablet. It was observed that the tablets containing maize starch and potato starch exhibited a higher percentage release in comparison with tablet containing microcrystalline cellulose.



In vitro data obtained for tablets containing paracetamol were used to determine the dissolution kinetics. The drug release data of paracetamol were fitted to various kinetic models. The data were processed for regression analysis using MS-EXCEL statistical functions. Evaluation of release kinetics and application of best fit by correlation coefficient shows that the drug release following Higuchi square root kinetics. The release exponent 'n' calculated from the Korsemeyer-Peppas equation, shows that in all the batches, the 'n' values were between 0.45 and 1. It can be suggested that the release mechanism was non-Fickian, anomalous transport where release dependent on both drug diffusion as well as polymer relaxation.

CONCLUSION

The present study was aimed at evaluating the disintegration property of and compares it with other synthetic disintegrant in the preparation of orally disintegrating tablets. The study showed that the Maize starch and potato starch have a better disintegrant property than the microcrystalline cellulose. It was concluded that maize starch and potato starch were having excellent superdisintegrant property which can be used as natural disintegrant in the tablet formulation.

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