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Diclofenac Tablet Formulation and Assessment Using a Novel Disintegrant Agent

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ABSTRACT

As a unique approach to drug delivery, the study's goal is to prepare and evaluate diclofenac tablets using natural plant seeds as a disintegrating agent. Six different kinds of natural plant—Lepidium sativum mucilage, mango peel pectin, Nigella sativa seeds, Hibiscus rosa sinenes mucilage, Plantago psyllium seeds, and dehydration banana powder were chosen for the study. The best seeds with the highest swelling index were chosen to be used as a disintegration agent in the formulation of Diclofenac tablets, and citric acid was used as a comparison disintegration agent. Various formulations were created utilizing the best disintegrating agent for tablet manufacture. The wet granulation process was used to make the tablets. Additionally, all tablet formulation is undergoing to test of in-vitro evaluation tests. The citric acid use to prepare diclofenac (T1) for compare. The results that obtain demonstrated the lepidium sativum seed and dehydration banana powder were chosen to prepare of Diclofenac tablets (T2, and T3) because of a good swelling index (230, 175) in pH 1.2 and (155, 125) in pH 6.8, and had good disintegration time (12.01±0.012, 13.28±0.52), friability (0.3 ± 1.5, 0.42 ± 0.16) and hardness (6.09±0.003, 5.99 ± 1.55) tests according to pharmacopoeia limited for T2, T3, respectively.

Keywords: Diclofenac tablet, Novel disintegration agent, lepidium sativum seeds, dehydration banana powder

I. INTRODUCTION

A tablet is a solid dosage form made up of one or more medications and excipients. It is a unit dosage form of medication that contains one or more medications and excipients that compress the pharmaceuticals into powder and granules with a certain shape. Due to its self-administration, patient convenience, and ease of manufacture, tablets are the most widely used solid dose form.[1,2] The selection of the right excipient is a crucial step in the formulation and preformulation of pharmacological dosage forms. The excipient's chemical, physical, and mechanical properties can have an impact on formulation parameters including shelf life, dissolution, and disintegration, which can have a significant impact on the finished product.[3] Excipients are defined as inert compounds that can be added to pharmaceutical preparations to provide desirable flavors and play a significant role in the production process and product stability.[4] Fillers, disintegrants, glidants, binders, antioxidants, lubricants, dissolving modifiers, absorbents, coloring agents, wetting agents, and preservatives are among the many types of excipients utilized in the creation of tablet formulations.[5] Disintegration agents are crucial ingredients in the manufacturing of tablets. The disintegration agent swells in the presence of solvent, causing the contents to be released from the tablet to form a soft, solid mass.[6] Disintegration agent action by different types of mechanisms for example of these mechanism swelling, heat of interaction[7] disruption the bonds between particles, strain recovery, and wicking.[8] Starch and its modified forms, sodium carboxymethyl cellulose and cross-linked polyacrylin, are the most common kind of disintegrants.[9] Furthermore, because they come from natural sources, are less costly, degradable, widely accessible, and environmentally

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benign, natural materials have advantages over synthetic ones.[10,11]

According to BCS, diclofenac belongs to class II. It is a semi-synthetic NSAID with high permeability and low water solubility that is used as an analgesic and anti-inflammatory. Diclofenac is used for a variety of illnesses to relieve pain, reduce swelling, and soothe inflammation, including rheumatoid arthritis, osteoarthritis, acute gout, and backaches. It works by inhibiting the COX enzyme and modifying the release and uptake of arachidonic acid.[12,13]

II. METHODS AND MATERIAL

Chemicals and Material used

The Sama Al-Fayhaa Iraq company was provided the Diclofenac sodium, while the natural plants seeds (Lepidium sativum mucilage, mango peel pectin, Nigella sativa seeds, Hibiscus rosa sinenes mucilage, Plantago psyllium seeds, and dehydration banana powder) were provided from Najef market, Iraq. Potassium dihydrogen phosphate, lactose, disodium hydrogen phosphate, HCL were purchase from BDH laboratory supplier, England.

Method

Process of Swell index:

Six types of plant seeds (Lepidium sativum mucilage, mango peel pectin, Nigella sativa seeds, Hibiscus rosa sinenes mucilage, Plantago psyllium seeds, and dehydration banana powder), Place 500 mg of each seed's grinding powder separately in a graduated cylinder. Then add gastric acid (pH 1.2) to bring the volume up to 3 ml. Then, record the powder's high throughout a 15-minute period. Use intestinal fluid (6.8 pH) to repeat the process.[14] Choose the seed powder with the largest swelling according to following equation:

$$swelling\ index = \frac{final\ volume - initial\ volume}{initial\ volume} * 100 \\ --1$$

Tablet preparation:

The Diclofenac tablet was formulated using the wet granulation process. prepared a batch of tablets for every type of different diclofenac and excipients mixtures (as indicated in table 1). Acacia was used as a binder, Acacia mucilage solution is made by dissolving acacia in warm water (20% w/v), then carefully weighing each ingredient using a digital balance[15], and the seeds were previously grinding with a mortar. Mix the ingredients (with half amount of disintegrating agent) around five minutes of thoroughly combining the powdered ingredients, add the acacia mucilage drop by drop to the mixture, mixing thoroughly for another five minutes, or until a wet mass is produced. The mixture is then sieved through a #8 mesh sieve to produce granules. then allowed to dry for four hours at 50 degrees Celsius in an incubator. After that, add a second half part the agent of disintegration and mix for five minutes. After sifting the mixture through mesh #30, the lubricating agent was added and mix for additional three minutes. Use a tablet machine to compress the mixture.

TABLE I: Diclofenac tablet formulas using potential disintegrant agent (n=100) for each formula

Constituent of tablet	T1	T2	T3
Diclofenac sodium (mg)	75	75	75
Acacia mg	6	6	6
lepidium sativum (mg)		6	
dehydration banana powder (mg)			6
Citric acid mg	6		
Steaic acid (mg)	0.6	0.6	0.6
Talc powder mg	1.2	1.2	1.2
Lactose mg	31.2	31.2	31.2

Evaluation of tablet

The prepared Diclofenac tablets were undergoing to in-vitro evaluated for friability, hardness, disintegration, and weight variation test

Hardness test

Hardness test

For this test, six tablets were chosen. The tablet's hardness was measured using an Erweka hardness tester. Hardness is the amount of force needed to crush a tablet between two jaws that are pushing against one another, in which one of the jaw move in the direction toward the other jaw. A mean hardness was determined.[16]

Friability test

Tablets' resistance to handling, shipping, abrasion, and packaging is assessed using the friability test. Twenty

tablets were chosen randomly, weighted using sensitive balance and placed in a Roche friabilator from Erweeka. The tablets were then exposed to two different types of effects—abrasion and shocks—using a plastic chamber spinning at 25 rpm for four minutes. The twenty tablets are then gathered, brushed clean, and weighed. Next, determine the weight loss percentage.[17]

$$friability\ test = \frac{final\ weight - initial\ weight}{initial\ weight} * 100$$
$$--2$$

Disintegration test

The disintegration test was used to calculate the time needed for the tablet to completely break down in the medium. The Erweeka company's disintegration equipment was utilized; it consisted of a stainless steel basket with six open-ended glass tubes supported vertically on a 10-mesh. Six tablets must be chosen at random and placed in each of the six basket tubes in order to conduct this test. After that, the basket moves mechanically up and down at a rate of 29–32 cycles per minute in the immersion fluid. Unless the individual monograph specifies differently, the temperature is kept at 37 °C.[16] The Simultaneous Intestinal Fluid SIF (6.8 pH.) and simultaneous Gastric Fluid SGF (1.2 pH.) were used as a media for this test.

Weight variation

The test of weight variation was done using (20) tablets, and sensitive digital balance was used to weight the tables individual and the average weight were also measured, and weight variation was measured using the following equation:

$$weight\ variation = \frac{individual\ weight - average\ weight}{average\ weight} * 100$$

----3

Statistical Analysis

All of data repeated, and the findings are expressed as mean ±SD. Microsoft Excel was used to do an ANOVA analysis on the data. The p <0.05 indicates statistical significance.

III. RESULTS AND DISCUSSION

Swelling index

Six natural plant seeds were assessed using the swelling index. Fig. (1) and Table (2) displayed the swelling index of six different plant seed types: Sinopis arvensis, Petroselinum crispum Lepidium sativum mucilage, mango peel pectin, Nigella sativa seeds, Hibiscus rosa sinenes mucilage, Plantago psyllium seeds, and dehydration banana powder. According to the results, Lepidium sativum seeds and dehydration banana powder exhibit a high swelling index at pH 6.8 and pH 1.2, indicating a higher capacity for water absorption and swelling properties. Additionally, these seeds also function well as disintegrants when used to formulate tablets[18], so these two type of seed were selected for formulation of tablet.

TABLE II: The seeds of natural plant powders and their swelling index in two media pH 1.2 and 6.8

Plant seeds	Quantity added mg	Swelling index pH1.2	Swelling index pH6.8
Lepidium sativum	500	230	175
Petroselinum crispum	500	130	19
dehydration banana powder	500	155	125
Hibiscus rosa sinenes mucilage	500	120	75
Nigella sativa seeds	500	175	30
Sinapis arvensis	500	215	19

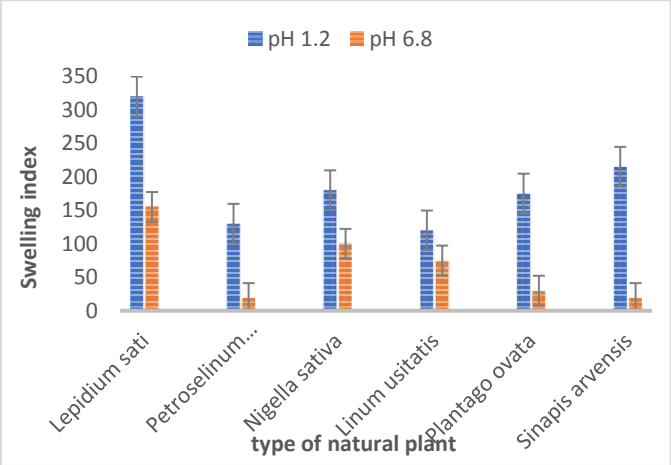

Fig. 1: Swelling index of seeds of the natural plant (Lepidium sativum mucilage, mango peel pectin, Nigella sativa seeds, Hibiscus rosa sinenes mucilage, Plantago psyllium seeds, and dehydration banana powder) in two media (pH 6.8 and pH 1.2).

Evaluation of tablets

Hardness test

The Hardness test for three formulas was done, as appear in table 3, T1 for citric acid, T2 for lepidium sativum seed, and T3 for dehydration banana powder, furthermore, the average hardness was recorded. The hardness in (kg/cm^2) was expressed in the result. According to the earlier study, a tablet's disintegration time increases as its hardness increases.[19]

Disintegration time

Table 3 shows that all formulations within the acceptable range disintegrated in less than 30 minutes. the time of breakup. Fluid seeping through the tablet's pores causes the disintegrant to swell and create hydrodynamic pressure, which ultimately causes the tablet to break.[18]

Friability test

Every formula underwent a friability test; as shown in table 3, all of the formulas have a percentage of friability below 1%, indicating that they have strong mechanical resistance and can withstand abrasion during handling, shipping, and packaging.[20,21] The maximum friability (0.78%) for T1formula and the minimum friability (0.3%) for T2 formula.

Weight variation

The limit of this test according to USP which indicate the accepted percentage of deviation for T1(n-20) its 168mg is (7.5%), while for T2, and T3(n=20 for each one) is 125 mg (10%), so formulas of tablets are accepted according to these result as show in table 3.

TABLE III: Evaluation tests of Diclofenac tablets for (T1, T2, and T3) formulas±SD

Formula	hardness (kg/cm^2)	friability %	Weight variation %	Disintegration min
T1	4.85±1.79	**0.78**± 0.16	0.78 ±0.002	4.65±0.004
T2	6.09±0.003	0.3± 1.5	0.52±0.01	12.01±0.0121
T3	5.99± 1.55	0.42±0.16	0.64±0.01	13.28±0.53

IV. CONCLUSION

The tablets of Diclofenac were effectively prepared by the method of wet granulation with using natural seeds of plant (Lepidium sativum and dehydration banana powder) as disintegrating agent, without any capping, chipping and sticking. The seeds of plant of Lepidium sativum and dehydration banana powder, appear with a good index of swelling (230, 175) in pH 1.2 and (155, 125) in pH 6.8, respectively. Using these natural disintegrate agent to prepare Diclofenac tablets show a good in-vitro evaluation tests, the time of disintegration was <30 min., and friability test <1% which refer to a good mechanical strength and, also hardness test results that are all within acceptable limits.

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