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DESIGN ASSESSMENT OF MATRIX TABLETS WITH INCLUSION COMPLEX & ROLE OFEGG SHELL POWDER AS A RATE CONTROLLER

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ABSTRACT

Aceclofenac's poor solubility in water was improved by the use of an inclusion complex with hydroxy-Cyclodextrin. Eggshell powder (ESP) was explored for the new application as pharmaceutical excipients and a rich natural source of calcium. The inclusion complexes were created using drugs to cyclodextrin (CD) ratios, 1:1, 1:2, and 1:3. Comparing the outcomes of all 3 formulations, the 1:2 drug-cyclodextrin combination produced superior outcomes. Matrix tablets were prepared by using Drug-Cyclodextrin inclusion complex and egg shell powder (F1-F4) by the direct compression method. The USP Dissolving Apparatus II was used to examine the *In-vitro* activity of all formulations in pH 6.8 buffer. Multiple physical evaluation tests were used to evaluate the formulation of the matrix tablets. The hydrophobicity of the modified ESP depends on type of solvent employed in the surface alteration process, which may explain about drug's extended release. After chloroform treatment, the sustained release profile of eggshell powder was higher.

Keywords: Aceclofenac, hydroxy-Cyclodextrin, Eggshell powder, Matrixtablets, Sustainedrelease

1. INTRODUCTION

Aceclofenac (BCS Class II medication) is atraditionalNSAID utilized in the rehabilitation of inflammation and joint pain that works by multiple processes **[1]**. These BCS class 2 medications often have high permeability and low solubility **[2]**. Drugs that are poorly water soluble (BCS class 2)

are typically associated with sluggish drug absorption, which ultimately results in insufficient and unpredictable bioavailability. Through inclusion complexation, cyclodextrins have capability to increase the solubility of substances that are not water soluble. The size of the central cavity of cyclodextrins, which have a stiff structure and 'tapered-like' or 'bucket-like' doughnut shaped molecules, varies depending on the type of cyclodextrin. The outside portion of the molecule is hydrophilic while the inside surface of the cavity is hydrophobic due to the arrangement of hydroxyl groups within the molecule. Because of its configuration, cyclodextrin can accept a visitor molecule and incorporate it into the cavity to create an inclusion complex **[3]**.

RA is a multisystem, chronic inflammatory illness with no known cause. Its hallmark is persistent synovitis that affects largely the peripheral joints symmetrically. This inflammation progresses to cartilage degeneration, bone erosions, and ultimately manifests as joint malformation **[4]**. Lack of nutrient supply can cause osteoarthritis, in which the bones weaken dramatically. Calcium helps to build strong bones and promotes the growth of new bone tissue, so consuming enough of it can lower the risk of osteoarthritis **[5]**.

A bio-waste material called eggshell (ES) is sourced from bakeries and fast-food outlets. This trash is typically dumped in landfills, endangering human health and harming the environment. Finding a different technique that may turn used eggshells into a useful product and aid the competitive egg processing sector financially is important. In addition to providing producers with a new source of income, it would aid in addressing the issue of high disposal costs and environmental issues. Sometimes, the used eggshells are used to the ground as a source of fertilizer. Numerous studies have investigated ways to make use of the eggshell waste, such as employing eggshell powder as a stabilizing substance to enhance the qualities of soil, as food additives, coating pigments for ink-jet printing paper, suppliers of calcium for both human and animal nutrition **[6]**.

Eggshell powder (ESP), which contains significant calcium, can be blended with pozzolanic materials like fly ash, which contain little calcium **[7]**. Egg shell powder is a natural, inexpensive supply of calcium in the form of $CaCO_3$, since calcium carbonate makes up a large portion of eggshells, it can be used to substitute calcium carbonate, a pharmaceutical excipient used in solid dosage forms and it also contains trace amounts of magnesium, potassium, zinc, and phosphorus **[8]**. egg shell powder has the ability to treat connective tissue and joint diseases **[9]**.

The primary goal of treatment is to enhance solubility and non-toxic for a long time and

achieve a steady state blood level. An essential component of achieving this goal is creating appropriate dose regimens. It is the goal of sustained release dose forms to distribute the medication at a controlled, maintaining a therapeutically effective medication concentration within the systemic circulation for a considerable amount of time at a predetermined rate, the improving patient acceptance and dosing intervals **[10]**.

2. MATERIALS AND METHODS

Aceclofenac is purchased from Fisher scientific, Mumbai, methanol, lactose obtained from Fisher scientific, Mumbai, and Hpmc purchased from Loba chemie Pvt. Ltd. βCyclodextrin from Cadila Pharmaceuticals, Ahmadabad. Magnesium stearate and Talc obtained from SD fine chem. Ltd, Chennai. Povidione k30 is Loba chemie laboratory reagent colabo, Mumbai.

2.1 Formation of inclusion complexes (Table 1)

Cyclodextrin was combined with just a little of water in a glass mortar to create a homogenous mass. Then, while grinding, aceclofenac was gradually added. The mixture was ground for an hour while receiving the correct volume of water to maintain the desired consistency. The resultant was dried in a 40° C oven for 48 hours **[11]**.

Table 1: Formulation table of inclusion complex

FORMULATION CODE	DRUG: CARRIER	DRUG	CARRIER
F1	1:1	1mg	1mg
F2	1:2	1mg	2mg
F3	1:3	1mg	3mg

2.2.1 Preparation and treating of Eggshell particles

The eggshell was properly cleansed with tap water once the membrane had been removed and boiled for 30 minutes in demineralized water. It was dried approximately 2 hrs in a hot air oven at 80°C. Using a clean and dried mortar and pestle, the eggshells was crushed until become fine powder. The investigation employed eggshell powder that had passed 200 mesh sieves **[12]**.

2.2.2 Treating of egg shell particles

20 g of eggshell fragments were treated with a 1.0% w/v stearic acid (20 ml) in either water, chloroform or 95% ethanol in a mortar. In the situation of water, steaming water was used, and the specimen was dried for a considerable amount of time at a temperature of 45°C in an oven. For the research on chloroform and ethanol room temperature was used, and the samples were left remained all night **[13]**.

2.3 Preparation of Matrix Tablets (Table 2)

By using direct compression method, matrix tablets containing aceclofenac-cyclodextrin complex were created. According to the formulations, the weights of the excipients

and active component were precisely calculated for 35 tablets. In a compact drum blender built for a laboratory, precisely weighed components were combined. Through mixing and phase homogeneity, special care has been taken to assure. The finished mixture was compressed using a tablet punching machine that was equipped with a cylindrical shape die and punch. Tablet's breadth and length are determined by the die and punches used to create it. So, following formulation, a round cylindrical shape was discovered in the tablet's internal morphology under an optical microscope **[14]**.

Table 2: Formulation table of Matrix tablets

INGREDIANTS	F1(mg)	F2(mg)	F3(mg)	F4(mg)
Drug:cyclodextrin	300	300	300	300
HPMC	75	75	75	75
Un-treated ESP	150	-	-	-
Water treated ESP	-	150	-	-
Ethanol treated ESP	-	-	150	-
Chloroform treated ESP	-	-	-	150
Lactose	100	100	100	100
Magnesium stearate	5	5	5	5
Povidone k30	100	100	100	100
Talc	5	5	5	5
TOTAL	735	735	735	735

3.1 EVALUATION

3.1.1 Calibration of aceclofenac inMethanol

10 mg drug dissolved in 10 ml solvent, it becomes 1000ug/ml solution. From this pipette out 1 ml and makeup to 10 ml with solvent, this becomes 100ug/ml solution. From this again pipette out 1 ml and makeup to 10milliliters, this was 10ug/ml solution. From 10ug/ml solution make different concentrations and the absorbance scanned at 275nm **[15]**.

3.1.2 Assay

100 mg of drug was placed in a 100 ml graduated flask. The required amount of methanol was added to make the volume correct. Whatman Filter Paper No. 41 was used to filter the mixture. Transfer 5 ml of filter into a 50 ml volumetric flask and dilute it with solvent. The sample was divided into 1 ml aliquots, diluted to a strength of 10 g/ml with Methanol. At 275 nm Absorbance was scanned with Methanol used as the reference. Calibration graph approach was used to determine the drug's purity percentage.

3.1.3 FTIR

A common identifying parameter for understanding the chemical makeup of medications is the infrared spectrum. All ingredients FTIR spectrum was obtained using an FTIR spectrophotometer. A small amount of the specimen was mixed with just enough KBR and compressed into a pellet using a hand-operated press at a 10 tons pressure. This pellet was scanned from 4000

to 400 cm-1 while it was contained in a sample container **[16]**.

3.1.4 Phase solubility study

To find out how the cyclodextrin complexes affect the solubility of the Aceclofenac, phase solubility tests for ACE complexes were conducted. These investigations also yield the stoichiometry of drug:cyclodextrin complexes and the numerical values of their stability constants.

Procedure: In order to conduct phase solubility studies on ACE, a large quantity of the drug (200 milligrammes) was added to 20 ml portions of distilled water, each of which had varied concentrations of - cyclodextrin, including 0, 1, 3, 6, 9, 12, and15 × 10 moles/liter. For 72 hours, various concentrations of CD were shaken in the solutions. After being shaken, the solutions were filtered andassessed at 275 nm. On the basis of the computation of the solubility of ACE in each cyclodextrin solution, a phase solubility diagram between the solubility of ACE and different cyclodextrin concentrations was produced **[17]**.

3.1.5 *IN-VITRO* activity of inclusion complexes

Aceclofenac inclusion complex *in-vitro* study was investigated in USP XXIV dissolution apparatus type-1 and900 ml of distilled water was used as the dissolving media. The rotational speed set to 50 rpm. The dissolving medium was earlier warmed to 37.5° C and kept at that temperature for the duration of the experiment. At predetermined intervals, 1 ml of the dissolution media sample was taken out, filtered, and after being properly diluted with distilled water, the samples were tested for drug release via estimation of the absorbance at 274 nm. The fresh distilled water was then added to replace the volume that was withdrawn at each interval. Aceclofenac release % was calculated and shown against time **[18]**.

3.2. PRE-FORMULATION STUDIES

3.2.1 Flow rate

The distance between the tip of the dry plastic funnel and the table was 5 cm, and the funnel was supported by a retort stand. Under the funnel assembly, a piece of paper was inserted. The funnel outlet was covered with a layer of fiber board. The powdered mixture was then added in 10g portions into the funnel without being compacted. The timer began running as soon as the fiber board sheet was removed. Once all of the powder had been poured down the funnel, the timer was stopped. It was timed how long it took the powder to flow completely out of the funnel. The study was carried out in triplicate for each batch of granules, and the mean was calculated **[19]**.

Flow rate = weight of powder / time of flow

3.2.2 Angle of Repose

Angle of repose was calculated using the fixed funnel method. A sterile, dry funnel

was kept upright in a retort stand at a distance of 5 cm above a paper that was laid on a level, horizontal surface. After blocking the aperture, 10 gm of the powder sample were poured into the funnel. Whenever the funnel was opened, the granules was released onto the paper and formed a conical pile. Two rulers were used to gauge the height of the stack. The cone's diameter was measured and recorded on the paperandwith a pencil, the foundation of the powder was traced. For each batch of granules, the experiment was conducted three times, and an average was determined **[20]**.

$$\mathbf{Tan\ \Theta = h/r}$$

h-Hemp height,
r-Radius of the powder.

3.2.3 Bulk Density

The granules were measured at 10 gm and then put into a graduated cylinder measuring 100 ml. Vo, the inaugural volume, was recorded. Each batch of granules had this determination made in triplicate, and the average was computed **[21]**.

$$\mathbf{BD = W/V_o}$$

Where BD is bulk density,
W -weight of granule
V_o is bulk volume.

3.2.4 Tapped Density

Mechanical tapping was performed on a 100 mL graduated cylinder containing 10 grammes of the granules by lifting the cylinder and allowing it to fall to the ground under its own weight. The cylinder was tapped 100 times on a sheet of paper that was spread out on the lab workstation to obtain an equal amount of powder. The amount of space the powder took up was noted. Each batch of granules underwent this evaluation in triplicate, with the average being computed **[22]**.

Tapped density (TD) =Powder weight/tapped volume

3.2.5 Hausner's Ratio

This was calculated as the difference between the bulk density and the tapped density for each batch of granules.**[23]**

Hausner's Ratio = tapped density of granules/bulk density

3.2.6 Carr's Compressibility Index [24]

carr's index = tapped density-bulk density of sample/tapped density×100

3.3 EVALUATION OF MATRIX TABLETS

3.3.1 Weight Uniformity Test

tablet made to have a certain quantity of the medication. The mass of the tablet is regularly measured during manufacturing to make sure it contains the appropriate amount of medication.20 tablets were randomly selected from every batch and their mean weight was calculated. The departure of each weight from the average weight was then determined, followed by the standard deviation **[25]**.

3.3.2 Hardness

The Monsanto hardness tester is made up of a barrel with a compressible spring inside, two plungers, and two plungers that are with the bottom plunger in contact with the pill, a

zero reading is then obtained. The upper plunger is finally forced up against a spring by spinning a threaded bolt, which breaks the tablet. As the spring is compressed, a pointer moves along a gauge in the barrel, measuring both the applied force and the force at which the spring cracked **[26]**.

3.3.3 Friability

From every batch, 20 tablets are picked at randomly and weighed. For 100 spins, the Roche Friabilator is employed to test the friability of tablets. The friabilator is turned on for 4 minutes @ 25 rpm. The medications are rotated while being dropped from a height of 6 inches and subjected to a plastic chamber that combines the effects of shock and abrasion. The samples were removed, sanitised and reweighed. A percentage (%) is used to express it. It is permitted to use tablets that are with less than 1% friability. The algorithm below was then used to calculate the percentage of friability **[27]**.

$$F=Wo-W1/Wo\times 100$$

W0 =initial mass of tablets before friability,
W1 =mass of the friable tablets.

3.3.4 Disintegration time

A single unit should be placed in every single one of the six tubes in the basket, and a disc can be added if required. Unless another liquid is indicated, operate the equipment with water as the immersion fluid and keep its temperature between 35 and 39°C. Discard the basket from the liquid when the given time has passed, then examine the dose units. They have all totally broken down. If one or two dosage units don't dissolve, repeat the test on 12 additional dosage units. The study is deemed to have been successful if at least 16 out of the 18 dosage units subjected to the test disintegrate **[28]**.

3.3.5 Thickness and Diameter

Tablet for measuring One of the physical evaluation processes is thickness, and this can be done with a tool called a vernier caliper. The vernier caliper provides readings in millimeters and has a digital display as well as manual reading options. Simply place the tablet between the jaws and slide the scale jaw to push the tablet against the stationary jaw to measure the thickness. It is noted that the reading on the display is the true thickness of the tablet **[29]**.

3.3.6 *In-Vitro* Release data

Utilising a USP type-II dissolution equipment having PH 7.4 buffer and a 50rpm rotation speed, in vitro dissolution investigations were carried out. The dissolving media was kept at 37°C plus or minus 0.5°C. To maintain sink conditions, at regular intervals, a portion (5 mL) was withdrawn and swapped with an equivalent quantity of the buffer. The drug concentration was measured via UV-visible spectrophotometer at 276 nm **[30]**.

3.3.7 Stability studies

Three months of stability testing were conducted on tablets at 40°C and 75% relative humidity. Stability of a

pharmaceutical preparation refers to the capacity of a certain formulations (dosage form or medicinal product) in a particular container/closure system to maintain its physical, chemical, microbiological, therapeutic, and toxicological requirements during its shelf life. Because it enables for the timely verification of satisfactory outcomes under pressure and rapid stability research is highly fascinating and enticing. It produces data on which recommendations for a drug's or dosage form's shelf life and suggested storage conditions are based. The drug content has not significantly changed. According to dissolution data, expedited stability trials lasting six months did not reveal any discernible changes **[26]**.

4.RESULTS

4.1.1 Assay:

The calibration graph approach (least square method) was applied to determine the drug's % purity. Results indicate that the API was 99.27% pure **(Table 3)**.

4.1.2 Calibration curve

Aceclofenac's UV absorption spectra in methanol exhibitsλ maxat 275 nm. **Figure 1** displays the absorbance for various aceclofenac doses. concentration versus absorbance graph was discovered to be linear in between the concentrations of 2 µg /ml to 10 µg /ml.

4.2.1 Phase solubility study of inclusion complexes

The phase solubility showed a linear association (r2= 0.991) between the rise in -cyclodextrin and the increase in aqueous drug solubility **(Figure 2)**.

4.2.2 Drug release of inclusion complexes

According to the *In-vitro* data, the kneading method's formulationF2 discharged the most medicineand gave the highest percentage of release within an hour, which was over 98.54% when compared to all other formulations **(Figure 3)**.

4.3 Pre-formulation studies

The primary step in creating tablet dosage form is granulation. A granule is an accumulation of its component particles that is held together by the presence of weak links. The qualities of the granules, including their shape, size, hardness, surface properties, and specific surface area, can have a big impact on how quickly the medications in the heterogeneous formulation dissolve. Granule pre-formulation information is included in **Table 4**. The outcomes demonstrate that the granules have sufficient flow properties.

4.4 FTIR & DSC

The ESP's FTIR results show peaks at 14133, 873, and 708, which clearly suggest that calcium is present and can be utilized as a natural calcium supplement **(Figure 4-9)**.

4.5 EVALUATION OF MATRIX TABLETS

The tablets of various formulations were put through a variety of evaluation tests,

including ones for hardness, friability, Disintegration, Weight variation (%). **Table 5** lists the outcomes for these parameters. For each of the four formulations, physical evaluation tests were carried out and the results were clearly indicated that all the parameters within the limits so all the formulations pass all tests.

4.6 *IN-VITRO* Dissolution:

Aceclofenac was utilized as a reference drug in this current investigation since it has a maximum at 275 nm. Aceclofenac's standard curve is shown in **Figure 10**. **Figure 10** depict the dissolving profiles of all four formulations over a 5-hour period. Recently manufactured untreated eggshell powder tablets, water treated, chloroform and ethanol treated treated eggshell powder tablets were all found to have a total percent drug release at 30 minutes that was 99.88%, 12.55%, 8.07%, and 7.34%, respectively. The percentage of drug release from tablets of eggshell powder treated with water, ethanol, and chloroform increased to 100%, 99.33%, 75.34%, and 77.05%, respectively, at 5 hours. For tablets made of untreated eggshell powder, a quick drug release was achieved that serves as an immediate release mechanism.

4.7 Stability studies

The In-vitro trajectory of water-treated ESP tablets exhibits a trend similar to that of chloroform and ethanol treated ones, with the exception that the extent or percent drug release from the water sample was larger than that of the other two samples. Additionally, **Table 6** showed the outcomes during a six-month period of storage at 45°C. According to the findings, all formulations' drug release patterns remained unchanged after six months of storage at 45°C. This might show that the formulations have good stability.

5. *IN-VIVO* STUDIES

5.1 Selection of Animals

• GROUP 1 - Control

• GROUP 2 – Negative Control - CFA

• GROUP 3 – Standard (diclofenac 100 mg/kg)

• GROUP 4 – Test (aceclofenac 100 mg)

5.2 Anti-arthritic activity

volumes of the paws as measured. The onset of rheumatoid arthritis in rats was visible after two weeks of CFA injection. There was a noticeable increase in paw size, erythema, edoema, joint stiffness, and mobility restriction. On the seventh, fourteenth, twenty-first and twenty-eighth days following CFA injection, paw volume was measured using a digital plethysmometer. the optimized formulation was reported to reduce the paw circumference from 73.32±0.17 mm in the CFA control group to 53.16 ±1.0 5 mm. In comparison to the CFA-control group, the test-induced reduction of paw volume was found to be statistically significant ($p = 0.005$).

Table 3: assay of aceclofenac

S. No.	%PURITY	AVERAGE
1	97.23	99.27%
2	100.18	
3	100.40	

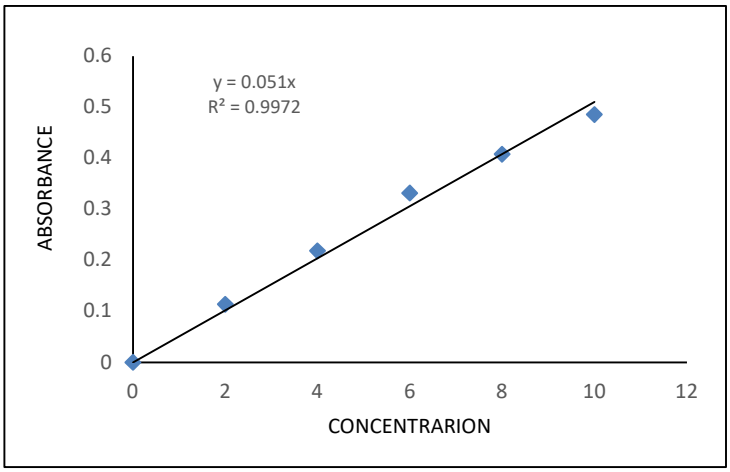

Figure 1: calibration curve of Aceclofenac

r^2 is 0.9904 so there is a positive co-relation between x-axis variables and y-axis variables

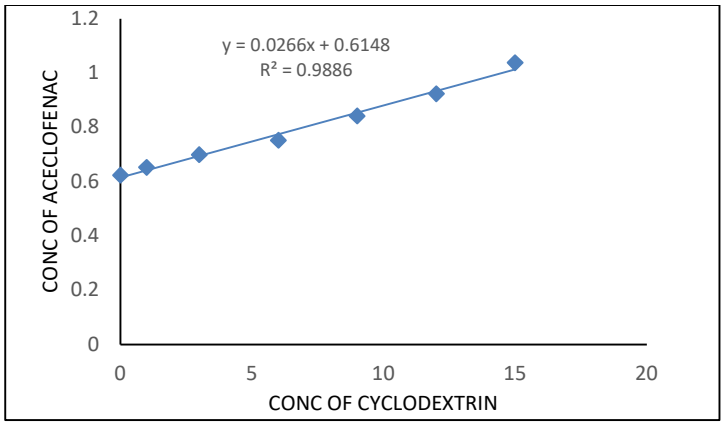

Figure 2: Phase solubility graph

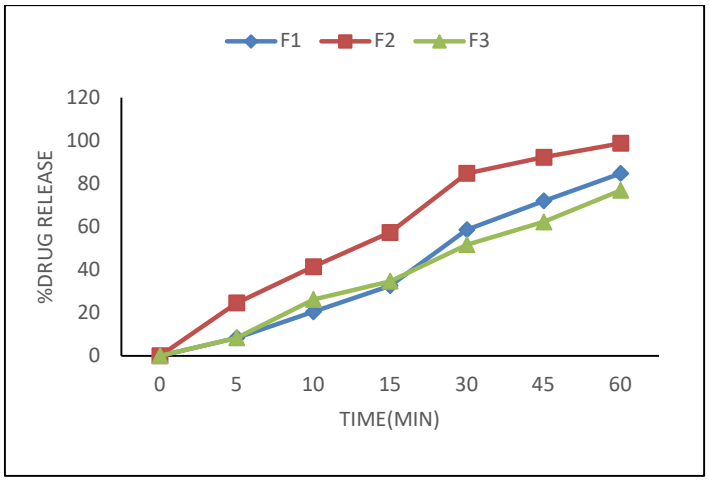

Figure 3: Characterization of inclusion complexes' drug release

Table 4: pre-formulation data

FORMULATION CODE	FLOW RATE	ANGLE OF REPOSE (o)	BULK DEENSITY (g/cm3)	TAPPED DENSITY (g/cm3)	CARR'S INDEX (%)	HAUSNERS RATIO
F1	12.14±0.52	24.93±1.77	0.59±0.000	0.67±1.84	14.07±1.43	1.18±0.034
F2	10.73±0.33	21.64±1.04	0.56±0.008	0.63±0.17	16.03±1.84	1.14±0.005
F3	14.82±0.47	23.81±0.01	0.55±0.004	0.66±0.04	12.39±1.22	1.19±0.02
F4	11.66±0.02	21.03±0.06	0.57±0.000	0.62±1.28	14.16±1.09	1.16±1.43

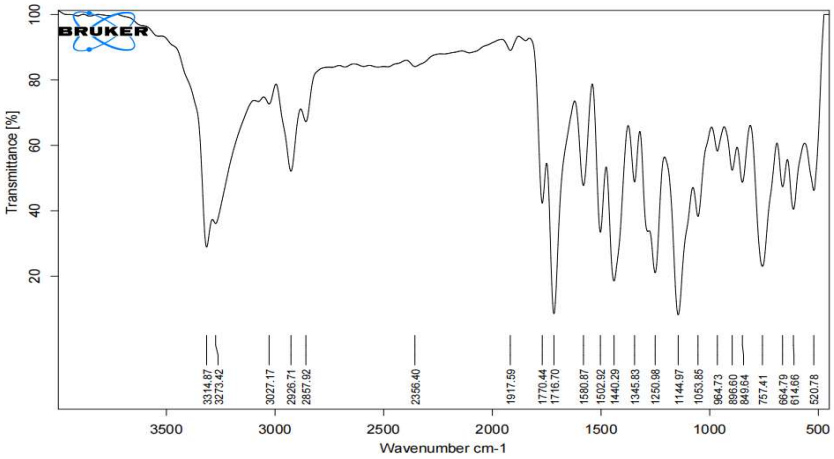

Figure 4: FTIR of aceclofenac

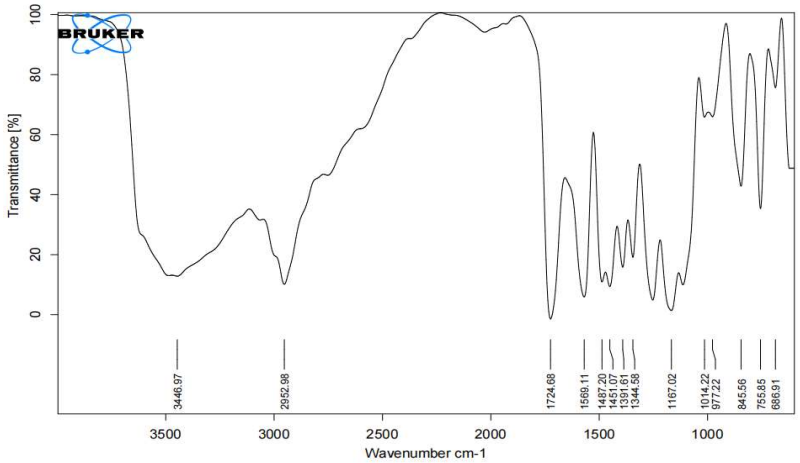

Figure 5: FTIR 0f DRUG + CD

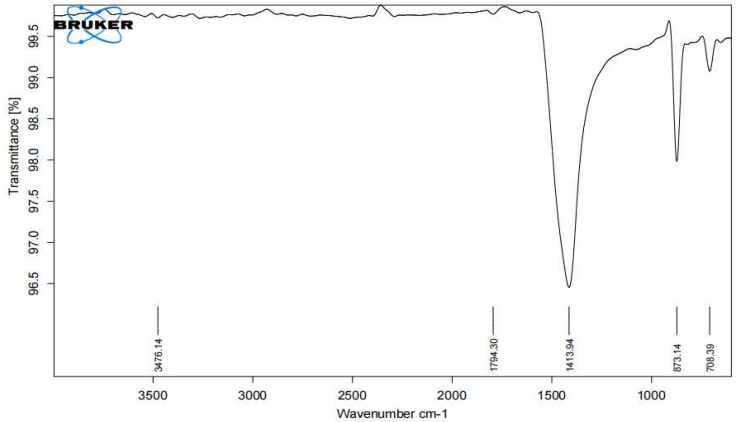

Figure 6: FTIR of Egg Shell Powder

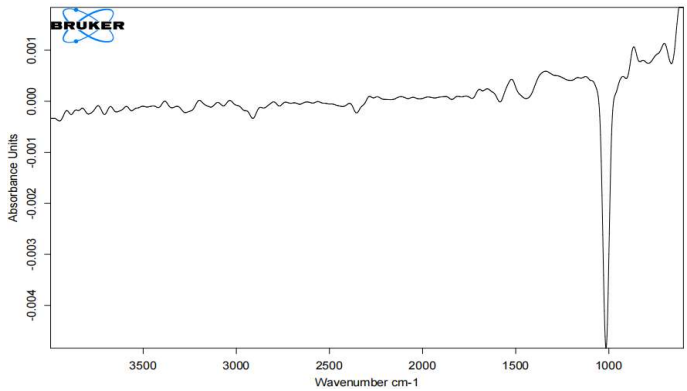

Figure 7: Formulation with ethanol treated egg shell powder

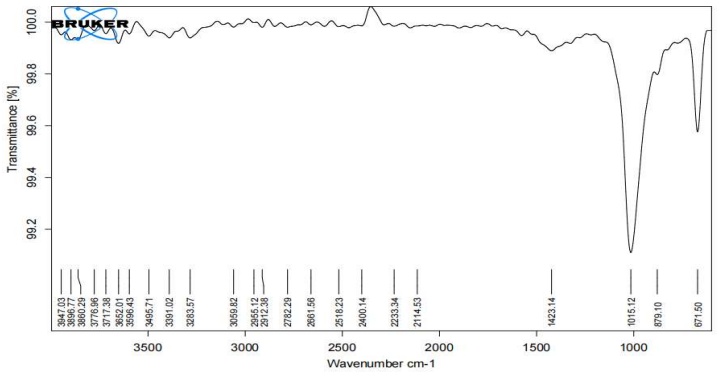

Figure 8: Formulation with chloroform treated egg shell powder

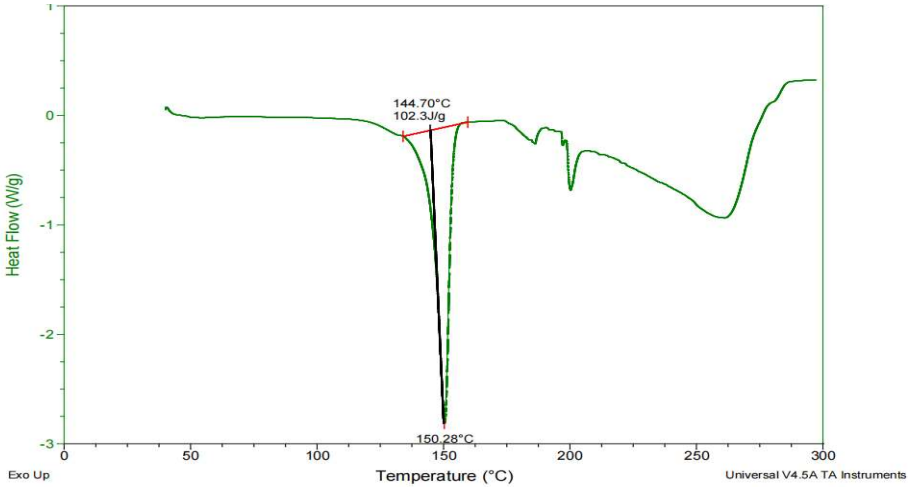

Figure 9: DSC of pure drug

Table 5: Evaluation of matrix tablets

EVALUATION TEST	F1	F2	F3	F4
Weight variation (%)	0.36±0.09	0.24±0.037	0.36±0.13	0.38±0.21
Crushing strength (Kg/cm2)	6.3±0.14	5.9±0.45	6.5±0.03	6.2±0.99
Friability (%)	0.5±0.55	0.4±0.19	0.5±0.62	0.3±0.36
Disintegration	15-20min	7-8hrs	7-8hrs	7-8hrs

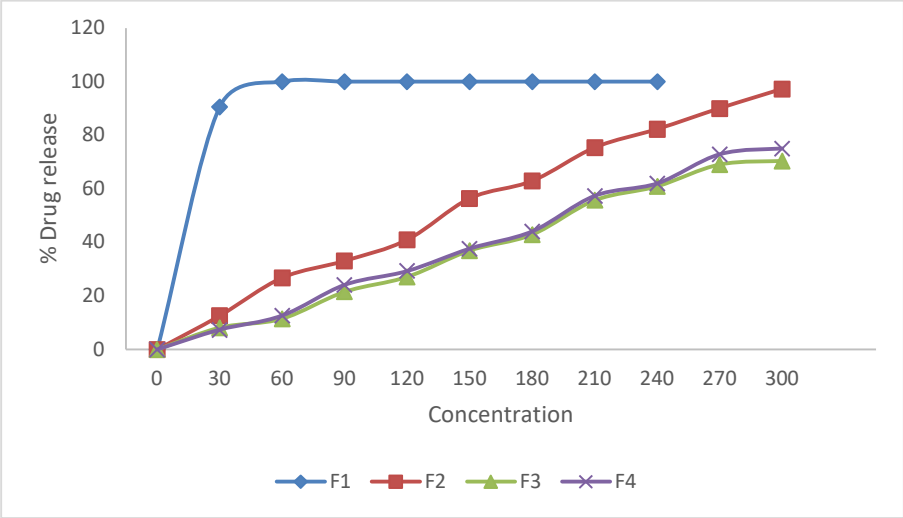

Figure 10: drug release of matrix tablets

Table 6: % Drug content

FORMULATION	0 MONTHS	3 MONTHS	6 MONTHS
F1	99.64±0.24	98.32±0.65	98.02±0.44
F2	99.52±0.53	98.03±0.87	97.85±0.16
F3	98.29±0.12	96.25±0.42	95.29±0.50
F4	99.35±0.94	97.51±0.77	96.94±0.39

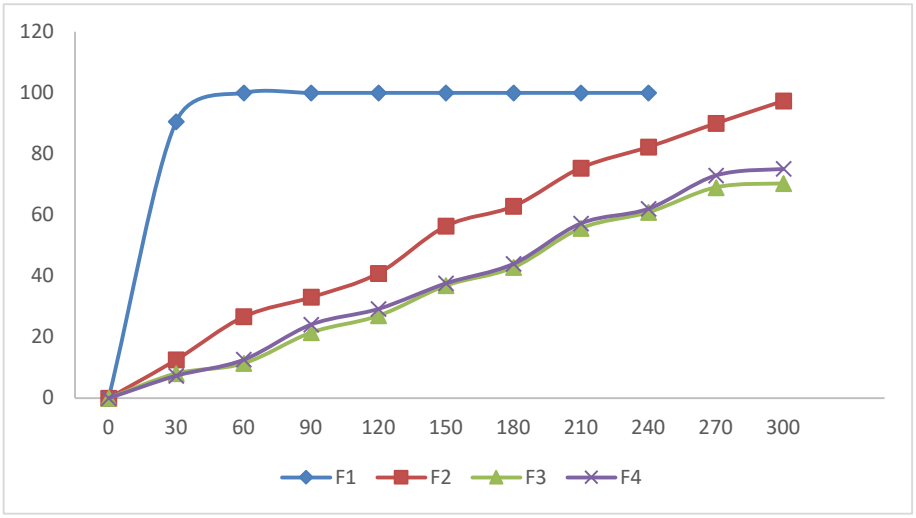

Fig 11: drug release after stability studies

Table 7: *In-vivo* data

Time (min)	Control	CFA (0.1ml)	Standard (diclofenac 100 mg/kg)	Test (aceclofenac 100 mg)
0	1.650±0.087	1.700±0.071	1.650±0.087	1.525±0.025
5	1.600±0.071	1.875±0.025	1.850±0.104	1.700±0.041
15	1.600±0.071	2.375±0.125	2.075±0.103	1.975±0.103
30	1.725±0.063	2.750±0.087	2.050±0.096	2.100±0.071
60	1.725±0.085	3.100±0.091	1.950±0.029	1.950±0.050

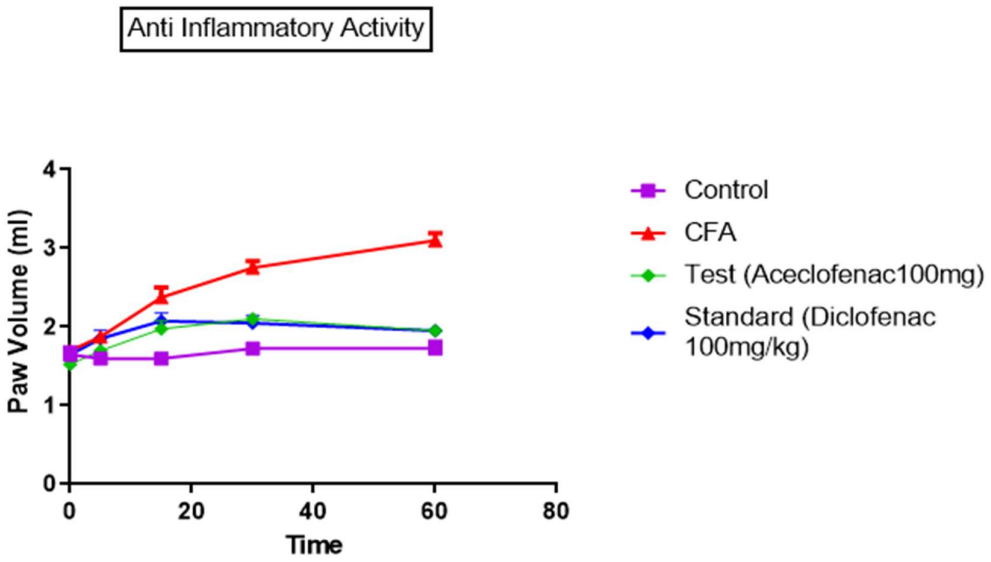

Figure 12: graphical representation of obtained *in-vivo* results

6. DISCUSSION

Aceclofenac was chosen as a model medicine for the study since it is used to treat joint discomfort (rheumatoid arthritis). It belongs to the BCS-2 class of medicines, which have poor solubility and high permeability. Solubility is a critical phase in medication pharmacokinetics. However, due to the low solubility profile of aceclofenac, Pharmacokinetics responses may be delayed in these cases. These poor solubility problems were solved using one of the most recent methods known as inclusion complexes. The medication (aceclofenac) was complexed with hydroxy propyl beta-cyclodextrin in this study.

These cyclodextrins have a form like a hollow, with the hydrophobic interior and the hydrophilic exterior. The regular distribution of glucose units in aqueous solutions allows aqueous solutions to form inclusion compounds. By replacing the water molecules in the central cavity using either the full drug molecule or more frequently, a lipophilic portion of the drug structure, many drugs can form complexes with cyclodextrins. The interior cavity is typically hydrophobic due to the presence of skeletal carbons and ethereal oxygen, whereas the cavity entrances are hydrophilic due to the existence of both primary and secondary hydroxyl groups. They have an enthalpy that is greater than the bulk of the solution's water molecules because they are unable to fulfil their hydrogen bonding potential. More hydrophobic species substitute the displaced water in the cavity. The cyclodextrin can contain molecules with the right size and stereochemistry thanks to hydrophobic interactions. The solvent of choice for complexation is water. As a non-polar in nature (hydrophobic)

guest or proton, it prefers the non-polar the atmosphere of the cyclodextrin cavity to the polar aqueous environment. As a result, water dissolves both the guest and the cyclodextrin while also acting as a catalyst for the complexation reaction.

Various drug:CD complex ratios were formed using the kneading process, and these complexes were evaluated using phase solubility experiments, in-vitro dissolution studies, and FTIR. Following the application of several assessment procedures to the resulting inclusion complexes, it was determined that the complex of drug:CD in the ratio of 1:2 was the best.

The matrix tablets formulation code was constructed utilizing this 1:2 ratio of Drug:CD complex, and different egg shell powders were incorporated. These eggshell powders are classified as untreated, water treated and chloroform treated, ethanol treated. FTIR analysis of the powdered eggshell reveals that it is rich in calcium which plays main role in the prevention of osteoarthritis. These egg shell powders were made by cleaning and crushing egg shells, and the resulting fresh egg shell powder was divided into four components. The first component was not treated, while the other three were, in that order, treated with water, ethanol, and chloroform. The direct compression method was used to create four sets of matrix tablets, which were labelled F1, F2, F3, and F4. All powder sets exhibit outstanding flow qualities, and the findings of pre-formulation investigations are well satisfied.

Different sorts of evaluation tests were performed on matrix tablets, and FTIR results reveal that there are no interactions. All of the results were positive, however this study concentrates on the effect of different egg shell powders. According to *In-vitro* dissolving data of F1, F2, F3, F4, untreated egg shell powder displays immediate release and medicine release within 30-45 minutes, however water treated egg shell powder takes up to 5 hours to release maximum API. Finally, drug release from ethanol and chloroform-treated eggshell powders is 75-80% within 5 hours. Finally, stability experiments were performed on all formulations, and the results reveal that there is no spoilage, degradation, or change in pharmacological characteristics during storage.

7. CONCLUSION

The study's findings allow for the conclusion that creating inclusion complexes using cyclodextrins can help poorly soluble medicines become more soluble. powdered form of eggshells can be incorporated into solid dosage forms as an excipient. It can be used in the formulation of tablets as a diluent and/or a medication release regulating agent and also a calcium supplement. The untreated powdered eggshell was appropriate for the fast release

formulation, but the treated particles were acceptable for controlled or sustained release formulations. After reviewing in-vivo data, it became evident that the water treated ESP formulation was an effective solution for the treatment of RA and has been non-toxic and safer to use. Regarding economic and environmental considerations, the water-treated approach was discovered to be the best way among the three formulations that had been treated.

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