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Assimilating Patrimonial Abortifacient Papain in the Form of Enteric Coated Tablet

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ABSTARCT
According to statistical findings, during 2019 to 21 there were 4.0% more reported abortions among urban women than rural women. In same period, about one-fourth (26.2%) of Indian women had at-home abortions. Synthetic abortifacient has adverse effects which motivates for researching herbals utility for the purpose. Papain is active constituent from Carica papaya proved to produce abortifacient effect but is unstable enzyme in dosage form and at gastric environment for oral administration. In requisition for the patient compliant formulation, present work included incorporation of papain into enteric coated tablet. Formulations were developed to find most stable method and compatible ingredients. Positive evaluation results suggested the in vivo study for the most stable formulation.
KEYWORD: Papain, enteric coated tablets, herbal abortifacient

I. INTRODUCTION

Worldwide, there are about 73 million induced abortions per year.[1]Products or substances used to end a pregnancy are known as abortifacients. Currently steroidal medications are used for the purpose like Mifepristone, Misoprostol etc. But it produces adverse effects like cramping, vaginal bleeding, fevers and chills etc. These have many adverse effects like obesity, heavy cramping, etc. For millennia, people have utilised herbal remedies to regulate fertility, offer contraception, or make abortion easier. Herbs and phytoconstituents are frequently preferred over synthetic medications because they are seen as "safe." Although there is relatively little available information describing the often-used plants and herbs, they have been utilised to cause abortions[2].Herbs like papaya, thuja, safflower etc, being safer are underutilised for the purpose of abortion, and can be researched.

According to WHO, induced abortion is a simple and common health-care procedure. Each year, almost half of all pregnancies – 121 million – are unintended; 6 out of 10 unintended pregnancies and 3 out of 10 of all pregnancies end in induced abortion[1]. When performed using a technique advised by the WHO, suitable for the stage of pregnancy, and by a qualified individual, abortion is safe. But when women with undesired pregnancies encounter obstacles to getting a good abortion, they frequently turn to risky abortion.Abortions may result in issues with the physical and emotional health of women, as well as social and financial pressures on communities and healthcare systems. Unsafe, untimely, unaffordable, and disrespectful access to abortion treatment is a serious matter of public health and human rights.Abortions may be induced through use of medicines or surgical procedures. It may be spontaneous due to genetic abnormalities, infection, vascular illness, diabetes, other hormonal issues, anomalies of the uterus, and lupus.

Historical background for abortifacients

Abortion has been carried out or attempted using a variety of methods, including the use of sharp objects, the application of abdominal pressure, the ingestion of plants that cause abortion.Although there is relatively little available information describing the often-used plants and herbs, that have been utilised to cause abortions.As long as there have been unintended pregnancies, women have tried to induce abortions with herbal medicines. Every culture appears to have its own unique blend.In both classical literature and folk medicine, there were numerous botanical concoctions thought to be abortifacient.One of the world's earliest medical writings, the Ebers Papyrus, describes an abortion method as a lengthy section on "remedies one prepares for women", with 70 entries covering the treatment of ailments like uterine prolapse, leukorrhea, breast disease, and irregular menstruation.A plant called silphium was well-known in Rome for its use as a contraceptive and an abortifacient in addition to its culinary and aromatic benefits.Women who want to cause an abortion are instructed to sit over a pot of

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steaming or simmering onions in an 8th-century Sanskrit manuscript.In the 11th-century poem-style herbal De viribusherbarum, a list of plants that cause miscarriage is given. Rue, Italian catnip, savoury, sage, soapwort, cyperus, white and black hellebore, and pennyroyal were a few of the plants that were there.

Current methods of abortion

Medicinal**:**Medical abortions are those induced by abortifacient pharmaceuticals. The most common early first trimester(12 weeks) medical abortion regimens use mifepristone in combination with misoprostol. Mifepristone–misoprostol combination regimens work faster and are more effective in the second trimester(12- 24 weeks).

Surgical: Up to 15 weeks' gestation, suction-aspiration or vacuum aspiration are the most common surgical methods of induced abortion. The surgical methods include:Manual vacuum aspiration (MVA), Manual vacuum aspiration (MVA), Dilation and curettage (D&C), Dilation and evacuation (D&E), Hysterotomy or Gravid Hysterectomy.

Labour induction abortion: An abortion can be induced by first producing labour and then, if necessary, by inducing foetal demise if a location lacks the medical expertise for dilation and extraction or when practitioners prefer it. This is referred to as an "induced miscarriage" at times.

Other Methods: Several plants that are said to have abortifacient effects have historically been utilised in folk medicine. Thuja, safflower, calendula, liquorice root, pineapple, and papaya are a few of them. Trauma to the abdomen can occasionally be used to attempt an abortion. If the force is great enough, it may result in catastrophic internal injuries without necessarily leading to a miscarriage.Misusing the medication misoprostol and inserting non-surgical objects like clothes hangers and knitting needles into the uterus are two reported dangerous, self-induced abortion techniques.

Mechanism of action of synthetic abortifacient

Mifepristone prevents the action of progesterone, by attaching to the intracellular progesterone receptor which causes the cervix and uterine arteries to dilate and cause uterine contractions.Misoprostol, on the other hand, attaches to smooth muscle cells in the uterine lining, which causes contractions to become stronger and more frequent, as well as to destroy collagen and lessen cervical tone.Misoprostol and mifepristone are combined in a regimen to abort pregnancies that are fewer than 70 days long. It functions by cutting off the hormone flow that keeps the uterus' inside in good condition. Without these hormones, the uterus is unable to support the pregnancy, and the baby is evacuated along with the uterus's contents.

Papain as abortifacient

Papain is extruded from the latex of raw Carica papaya i.e Papaya which is a small, sparsely branched tree, belonging to Caricaceaefamily, is a unique and traditional plant that is grown for its diverse medicinal and nutritive properties.

The unripe fruit contains a milky juice which contains a protein-digesting enzyme known as papain, which greatly resembles the animal enzyme pepsin in its digestive action.C. papaya contains flavonoids, phenolic compounds, alkaloids, and cynogenetic compounds in large amounts. It is wealthy with vitamins A, C, E especially in fruit and leaves which are the best antioxidants. Leaves and fruit are also loaded with minerals, Mg, K, and fiber. Papaya latex used is from the flower of male papaya with main compositions consisting of proteolytic enzymes, papain, glutamine cyclo-transferase, chymopapain A, B and C, peptidase A and B and lysozymes. The possible health benefits of consuming papaya include a reduced risk of heart disease, diabetes, cancer, aiding in digestion, improving blood glucose control, lowering blood pressure, skin and hair health anti-inflammatory activity [4], wound healing activity [5]. anti-fertility activity [6] [7], anticancer activity [8], antifungal activity [9]etc.

Crude papaya latex is valued in traditional medicine as an oxytocic agent (uterine contractant) used for labour induction and abortion. Native Asian people have reportedly used crude papaya latex applied intravaginally to the uterine opening to induce childbirth and cause abortion.An anti-fertility effect was noted on adult and pregnant rats. The activity of different components of Papaya fruit were investigated by different researcher. The result showed that unripe fruit of papaya disrupted the estrous cycle and caused abortion. It was also noted that as the fruit over ripened the effect on the estrous cycle decreased. It also has an effect in anti-implantation. Papaya helps in contracting the uterus muscles. Apart from producing heat in the body, the fruit contains carotene, which stimulates or regulates that oestrogen hormone levels in the body. Naturally, this induces bleeding or menses more frequently.

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Present article presents the assimilation of traditional abortifacient herbal medicine, papaya extract i.e. papain into oral tablet dosage form. Molecular docking was performed to confirm the relation between the abortifacient activity of papain molecule. Study was performed for formulating the enteric coated tablet containing papain which is unstable at gastric environment and storage. Systematic evaluation of the prepared formulation stressing the stability study was conducted.

II. MATERIAL AND METHODS

Papain (Carica papaya)was purchased fromHimedia Lab. Pvt. Ltd. Mumbai. Starch, calcium carbonate, povidone, magnesium stearate, microcrystalline cellulose was purchased from RanchemPvt.Ltd. Eudragit L100 was kindly gifted by academic research purpose.
Molecular docking was performed using MOE Molecular Operating Software.

2.1. Molecular docking

Molecular docking is a key tool in structural molecular biology and computer-assisted drug design. The goal of ligand-protein docking is to predict the predominant binding mode(s) of a ligand with a protein of known three-dimensional structure. Molecular docking is performed to confirm the abortifacient effect of papain with receptors responsible for abortion and exact binding site determination by docking score. Protein used for binding was found to be Lys 822.

2.2.Standardisation of raw materiali.e. Papain
Loss on drying

The test determines both water and volatile matter in the crude drug. Loss on drying is evaluated by the loss of mass evaporated as % w/w for 10 g of papain using hot air oven at 105°C for 5 hours, at the interval of continued and weighed to a constant weight at one-hour intervals.LOD was calculated using formula:
% Loss on drying = (Final weight of sample / Initial weight of sample) * 100

Ash Values

The ash content of crude drug is generally taken as the residue remaining after incineration. It usually represents the non-volatile inorganic salts like metallic salts and silica naturally occurring in the drug and adhering to it, but it may include inorganic matter added for the purpose of adulteration, contamination and substitution. This is an important parameter for the standardisation of crude drugs. The ash value can be determined by three different methods like total ash, acid insoluble ash and water-soluble ash. Each of these were performed in triplicate.

a. Total Ash: 2g of papain was incinerated in a tared silica crucible at 450ºC in a muffle furnace until carbon completely ashes and ignited to constant weight, removed, cooled in a suitable desiccator for 30 minutes and weighed. Percentage of total ash content was calculated with reference to the air-dried drug.
b. Acid Insoluble Ash: Ash obtained in total ash was boiled for 5 minutes with 25 ml of dil. HCl. Insoluble matter on an ash less filter paper is washed with hot water and ignited at 450ºC. Percentage of acid insoluble ash content was calculated with reference to the air-dried drug.
c. Water Soluble Ash: Total ash and 25 ml water, was boiled for 5 minutes and collected insoluble matter on an ash less filter paper. Washed with hot water and ignited in a crucible for 15 minutes at a temperature not exceeding 450°C. Water-soluble ash in mg per g of air-dried material was calculated.

2.2.3. Extractive value: Purity and amount of active constituents in a given amount of crude drugs can be determined by extracting the drug with solvents like alcohol and water.

a. Alcohol soluble Extractive: Macerated 5 g of the air dried, coarsely powdered drug, with 100 ml of ethanol (95%) in a closed flask for twenty-four hours, shaking frequently during six hours and allowed to stand for eighteen hours. Filtered and evaporated 25 ml of the filtrate to dryness in a tared flat bottomed shallow dish, dried at 105ºC to constant weight and weighed. The percentage of alcohol-soluble extractive value with reference to the air-dried drug was calculated.
b. Water Soluble Extractive: Procedure as mentioned for methanol soluble extractive value was performed using chloroform water instead of alcohol. The percentage of water soluble extractive value with reference to the air-dried drug was calculated.

Development of formulation

Granules preparation

The core tablets were formulated using the wet granulationmethod.Papain as API along with excipients maize starch, microcrystalline cellulose, calcium carbonate, povidone, magnesium stearate,

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were weighed and granulated. This leads to formation of a dough mass, which is used in the formulation of granules which are subsequently compressed in the form of tablets.

All the ingredients were accurately weighed as per formula in table and dispensed in clean polythene covers.

Ingredient	**Role in formulation**	**F-1 mg/tab**	**F-2 mg/tab**	**F-3 mg/tab**	**F-4 mg/tab**	**F-5 mg/tab**	**F-6 mg/tab**
Papain	API	200.00	200.00	200.00	200.00	200.00	200.00
Calcium carbonate	Diluent	2.00	2.00	2.00	2.00	2.00	2.00
Maize starch	Intragranular disintegrant	80.5	79.60	80.00	78.80	76.00	74.60
Microcrystalline cellulose	Diluent	44.00	45.00	45.00	46.00	48.00	49.50
Povidone	Binder	12.10	11.90	11.40	11.20	10.80	10.40
Purified Water	Vehicle	--	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.
Maize Starch	Disintegrant	7.80	8.00	8.10	8.50	9.00	9.80
Magnesium Stearate	Extracellular disintegrant	3.50	3.50	3.50	3.50	3.50	3.50
Tablet Weight		350.00	350.00	350.00	350.00	350.00	350.00

Table: Formulas for preparation of granules

Calcium carbonate, Maize starch, Microcrystalline cellulose were sifted individually through #100 sieve. Papain was mixed with Calcium carbonate and then sifted through #100 sieve. After sifting all the above intragranular ingredients they were transferred into a big polythene cover and mixed for 30 min. Binder solution was prepared by dissolving weighed amount of Povidone in required amount of purified water and added to the dry mix blend to granulate. Granules were dried in Fluidized Bed Dryer at 60°C & airflow 20 % till the LOD reaches below 2.50%. Moisture content was checked at 105°C for 5min. Dried granules were passed through #20 sieve.

Core tablet punching

The milled blend was mixed with pre-sifted extra granular Maize Starch. Pre-sifted Magnesium Stearate (# 80 sieve) was added to blend with a Turbula mixer (Analytical Technology, Bangalore, India) and mixed for 5 minutes at 12 rpm.The dried granules were mixed with drug and compressed on a 10-station tablet machine (Cadmach, Ahmedabad, India) using 10 mm round, standard concave die and plain punches. Three batches were prepared for each formulation.The average weight of tablets was also set according to the finished product specification. It should be 350mg limit ±5%.The weight, thickness and friability were adjusted at the beginning of the preparation and then, monitored every 15-minute during whole process of compression.Lubricated blend was compressed into tablets to meet the required standard physical parameters as given in Table and the compression was continued of the lubricated granules

Tablet coating

Seal coat of shellac was applied to the tablets up to a weigh gain of approximately 3%. Then the seal coated tablets were enteric coated with enteric coating polymer i.e.Eudragit L100 to protect the prepared tablets from acidic environment in the stomach. Then enteric coating was performed 6.74%.

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Figure: Coated tablet

Figure: Uncoated Tablets

Evaluation

Evaluation of Granules:

Granules were evaluated according to IP for flow properties, density, Hausner's ratio, Carr's and Index. Evaluation criteria is as mentioned in Tables.

Bulk density, Tapped density and Carr's index:

Ten grams of granules were introduced into a clean, dry 100 ml measuring cylinder and the volume was recorded. Th e cylinder was then tapped 25 times from a constant height and the tapped volume was read. Th e bulk density and tapped density were calculated as the ratio of the granules mass and the respective volumes. Carr's index (I) was calculated using the equation:

$I = Dt - Db / Dt \times 100$

Where,

Dt is the tapped density of the powder and Db is the bulk density of the powder.

Compressibility Index (%)	Flow Character	Hausner's Ratio
≤ 10	Excellent	1.00-1.11
11-15	Good	1.12-1.18
16-20	Fair	1.19-1.25
21-25	Passable	1.26-1.34
26-31	Poor	1.35-1.45
32-37	Very Poor	1.46-1.59

2.3.1.1. Angle of repose

The fixed funnel method was employed for determining the angle of repose. Th e granules were poured carefully until the apex of the conical pile just touches the tip of the stem of the funnel. Th e angle of repose was calculated using the equation:

$\tan \alpha = H/R$

Where,

H is the height of the pile and

R is the radius of the base of the conical pile

Angle of Repose	Type of flow
<25	Excellent
25-30	Good
30-40	Passable
>40	Very Poor

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Compatibility of ingredients

FTIR spectroscopy was performed to evaluate the API and excipients compatibility in the granules.Pure papain was considered as standard and was sieved through #100 sieves no for use. Sample was the prepared granules, which were triturated in mortar pestle and sieved through sieve no. #100. FTIR was performed for pure and formulated papain to identify any modification.

Evaluation of Core Tablet:

Core tablets were evaluated for parameters according to IP.

Uniformity of weight

Randomly selected twenty tablets were weighed individually and together in a single pan balance (Shimadzu, AX200, Japan). The average weight was noted and standard deviation calculated.

Sr.No.	Tablet Weight	IP Limit
1	80mg or less	10%
2	More than 80mg but less than 250mg	7.5%
3	25mg or more	5%

Table: Weight variation Specifications as per IP

Diameter and Thickness

Vernier Callipers was used to check the dimeters and thickness of tablets. Average was calculated.

Hardness

The tablet crushing strength was tested by commonly used Monsanto type tablet hardness tester (IEC, Mumbai, India). A tablet is placed between the anvils and the crushing strength, which causes the tablet to break, is recorded. Hardness was evaluated intermittently to confirm the desired range i.e. not less than 5kg/cm^2.

Friability

Tablet strength was tested by Roche friabilator (Electrolab, Bangalore, India). Pre weighed 20 tablets were given 100 revolutions in 4 min and were dedusted. The percentage weight loss was calculated by reweighing intact tablets. Ideally friability should not be more than 1%.Friability was calculated using following formula:

Friability = (W1−W2) / W1 * 100

Where,

W1= Initial wt. of tablets in gm

W2= Final wt. of tablets in gm

2.3.1.2. Disintegration Time

Disintegration time was determined using the disintegration apparatus USP (Electrolab, Bangalore, India) in acid stage emersion fluid i.e.0.1M HCl for 1h.If after 1 h no dosage unit shows evidence of disintegration, cracking, or softening, proceed with the Buffer stage. In buffer stage immersion fluid i.e.phosphate buffer pH 6.8 maintaining the temperature at 37 ± 2°C.

Drug content studies:

Phosphate buffer solution 5% was made with distilled water, which was used for further dilution. Standard stock solution with 1000 ppm was prepared for determining calibration curve. Subsequent dilution of stack solution was made to get 100 ppm solution which was further diluted to get different concentrations as 10,20,30,40,50 ppm for UV spectrophotometry using UV 150-02 shayd. Schimadzu spectrophotometer. The calibration curve versus absorbance was plotted and then straight-line equation was determined.

Five tablets from the prepared batch were weighed and crushed uniformly with the help of a mortar and pestle. An accurately weighed powder sample equivalent to 100 mg of Papain was transferred into a 100 ml of volumetric flask containing 5 ml of phosphate buffer. Sample was shaken to dissolve the content and then dilute up to 100 ml with water. Take 1ml dilute Phosphate buffer (5%) and dilute up to 10 ml with distil water [10] Absorbance was evaluated on UV 150-02 shayd. Schimadzu spectrophotometer and interpolated to check the concentrations from calibration curve.

Changes due to processing

FTIR spectroscopy was performed to evaluate the API and excipients compatibility in the granules. Pure papain was considered as standard and was sieved through #100 sieves no for use. Sample was the prepared tablet, which were triturated in mortar pestle and sieved through sieve no. #100. FTIR was performed for pure and formulated papain to identify any modification after the punching of granules.

Evaluation of Coated Tablets

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Weight variation Test

Randomly selected twenty tablets were weighed individually and together in a single pan balance (Shimadzu, AX200, Japan). The average weight was noted and standard deviation calculated.

Dimeter & Thickness

Vernier Callipers was used to check the dimeters and thickness of tablets. Average was calculated. Coat thickness was calculated from these values.

In vitro Dissolution Test

Dissolution Apparatus USP Type I Paddle type (TDT-08L, Electrolab, Mumbai, India) is used. Water bath is filled with water. Dissolution test was performed in gastric and intestinal pH conditions to confirm the proper release atmosphere for the papain. Vessel filled with 900ml of dissolution medium with 50rpm bath temp 37 °C. Withdrawal of 5 ml of sample with the help of pipette from vessel at an interval of 5 min. till 2hrs & after each withdrawal same volume i.e. 5 ml was added to maintain the sink condition. Filter the solution & makeup the volume up to 10 ml in volumetric flask.[10]The samples were analysed by UV spectrophotometer (UV 150-02, Double beam spectrophotometer, Shimadzu Corp.) at wavelength 278 nm.

a. Simulated Gastric Fluid (pH 1.2) Composition:

NaCl (3 g) was dissolved in about 1450 mL of DI water with continuous stirring and thenpH was adjusted to 1.2 ± 0.1 with diluted HCl.

b. Simulated Intestinal Fluid (pH 6.8) Composition:

Dissolving potassium phosphate monobasic (10.2 g) and SDS (3.75 g) in a same 1000 mL of DI water and then pH adjusted to 6.8 ± 0.1 with 1 N NaOH. Finally, the volume make-up of each prepared fluid.

Drug release kinetics

The drug release kinetics by different kinetic models for the optimum formulation (F2) was also studied.

Stability studies

The stability studies were carried out at 25°C ± 2°C / 60% ± 5% RH, 35°C ± 2°C / 60% ± 5% RH and 40°C ± 2°C / 75% ± 5% RH for selected formulations for 3 months.

Statistical evaluation

The data were statistically analyzed by one-way analysis of variance (ANOVA) and student's t-test.

III. RESULTS AND DISCUSSION

Molecular docking confirms the binding and interaction of papain molecule with the endometrial proteins site Lys822, which are responsible for contraction of uterus causing abortion of foetus. After confirming the positive results of docking score 0.9409. Table shows the run score for binding sites.

	mol	rseq	mseq	S	rmsd_ref...	E_conf	E_place
1	no-name	1	1	-6.2429	2.6810	-36.5861	-67.5246
2	no-name	1	1	-6.1731	1.4636	-36.7157	-81.6029
3	no-name	1	1	-6.1548	1.8150	-37.0825	-67.8477
4	no-name	1	1	-6.1419	2.2654	-37.0857	-79.6173
5	no-name	1	1	-6.1374	0.9409	-36.8412	-87.8096

Figure:Run scores for molecular docking

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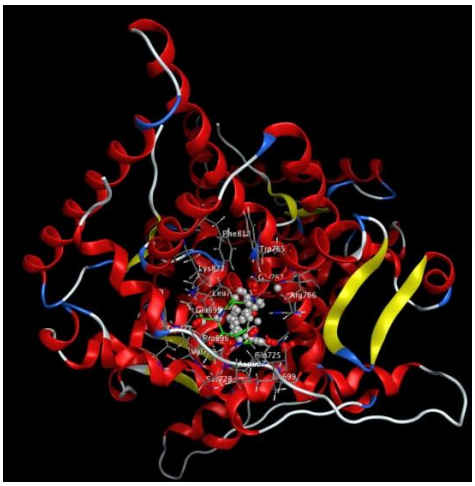

Figure 1: 2D binding site

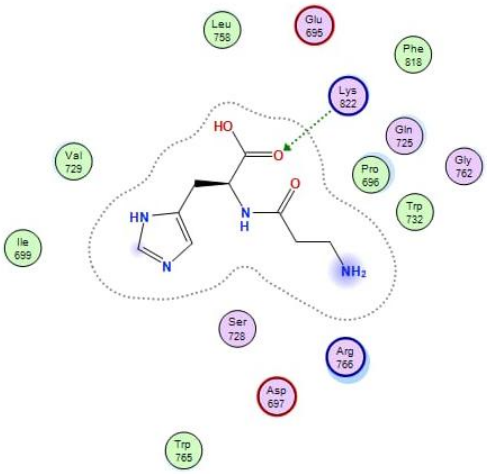

Figure 2: 3D binding site

Procured papain was amorphous or slightly granular,very light brownpowder with characteristic odour.Standardisation was carried out for evaluating the purity of procure papain which shown acceptable results as shown in table.

Sr. No	Parameters	Standard Criteria	Values Obtained (%w/w)
1.	Loss on Drying	NMT 12%	0.14
2.	Total Ash	NMT 10%	5.75
3.	Acid Insoluble Ash	NMT 2.5%	0.77
4.	Water Soluble Ash	NMT 5%	3.32
5.	Alcohol Soluble Extractive	NLT 6%	8.16
6.	Water Soluble Extractive	NLT 12%	28.2

Figure 3: Results for phsico- chemical evaluation

The compatibility studies to assess any possible interaction between the enzymatic drug papain and excipients were carried out and analysed using FTIR. The observed spectra did not show any alteration in peaks, suggesting no possible interaction between excipients and papain. As mentioned above, exposure of papain to acidic environment leads to significant degradation of the drug and reduces bioavailability as well. Enteric-coated tablets with a low core pH will have longer in vivo disintegration time, due to the suppression of ionization of enteric coating polymers in the acidic environment. Considering the dissolution in general and stability in particular, the pH of the core tablet was basified using sodium bicarbonate.Granule evaluation parameters with different formulations compared to find most suitable batch of granules for punching the tablet.
Based on the disintegration test, F6 formulation was selected for further enteric coating as this had shown minimum disintegration time 1.5 ± 0.30 min.The granules used for preparing the F6 formulations exhibited ideal properties for tablet compression like bulk density of 0.47 ± 0.05 g/cc, tapped density as 0.58 ± 0.03 g/cc, angle of repose as 29.65 ± 1.25 θ, Carr's Index as 18.96 ± 0.89. Physical properties of compressed tablets F6 exhibited good physical integrity like hardness was 5.6 ± 0.42 kg/cm2, friability was 0.27 ± 0.06%, weight variation: 351.95 ± 5.83, diameter 10.3 mm ± 0.05% and thickness of . Further, the core tablets F6 were seal coated with a commonly used polymer,Shellac up to 2.5 % w/w as seal coat. In general, these substances are anionic polymers or copolymers like Eudragit L100 are insoluble in acidic media but acquire water solubility at near neutral pH values due to ionization of functional groups along the polymer chain.Enteric coating of approximately 8% w/w.The weight variation and the drug content of all the formulations were found

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to be with-in the official limit. However, the formulations failed the disintegration test in 0.1 N HCl. Dissolution analysis was employed to assess the effect of the enteric coat composition and coverage levels on the release of the formulations.

Calibration curve was plotted to validate the concertation in formulation at wavelength 278 nm. Absorbance was observed at 0.123. In vitro drug release was carried out for formulations with 8% weight gain of enteric coated tablets of batchF6 in 0.1 N HCl for 2 h followed by phosphate buff er (pH 6.8) for 45 mins.The cumulative percentage released at the end of the study was found with acceptable range with formulation F6 made by enteric Eudragit L-100.

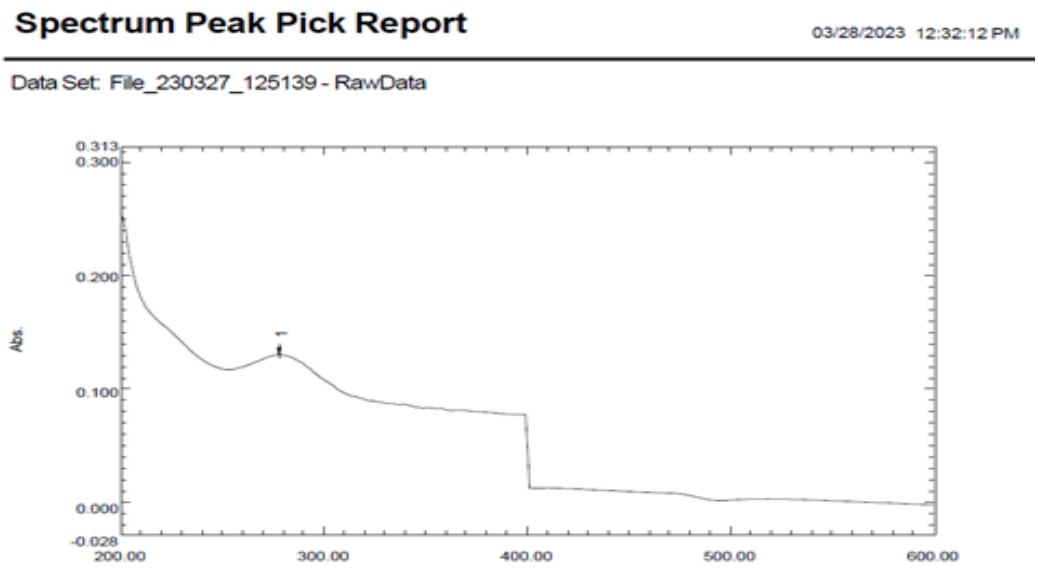

Figure 4: Wavelength Determination

Determination of Calibration Curve:

Sr.No.	Concentration	Absorbance
1.	10ppm	0.0789
2.	20ppm	0.079
3.	30ppm	0.0858
4.	40ppm	0.0958
5.	50ppm	0.0974
6.	Sample	0.1180

Calibration curve readings
From Linear regression Equation,

Concentration of Papain in one tablet of 350mg is found to be 147.2mg and percentage Purity of Papain in one tablet is found to be 73.6% w/w.

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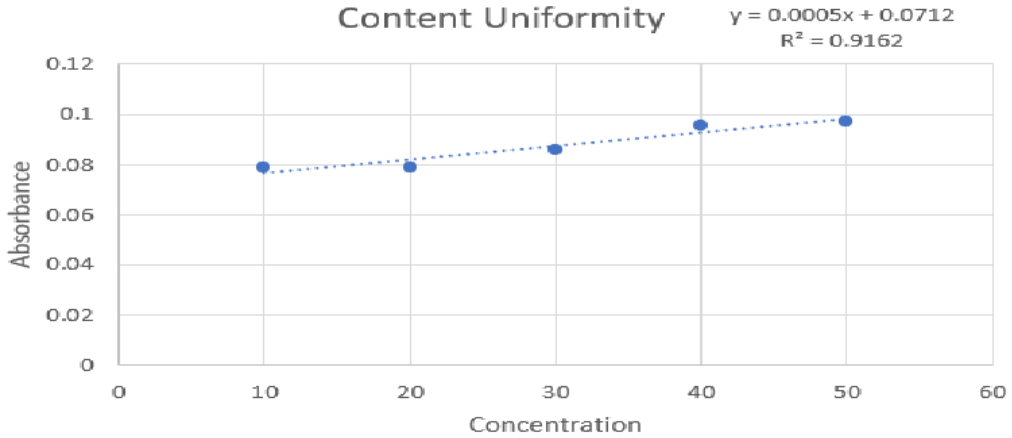

Figure 5: Content Uniformity

Time	Absorbance	Concentration	% Drug Release
5 min	0.0725	2.7776	12.5%
10 min	0.0728	3.2424	42.5%
15 min	0.0732	4.100	82.5%
20 min	0.0749	7.532	119.8%

Table : Dissolution and drug release readings

FTIR Spectroscopy Analysis:

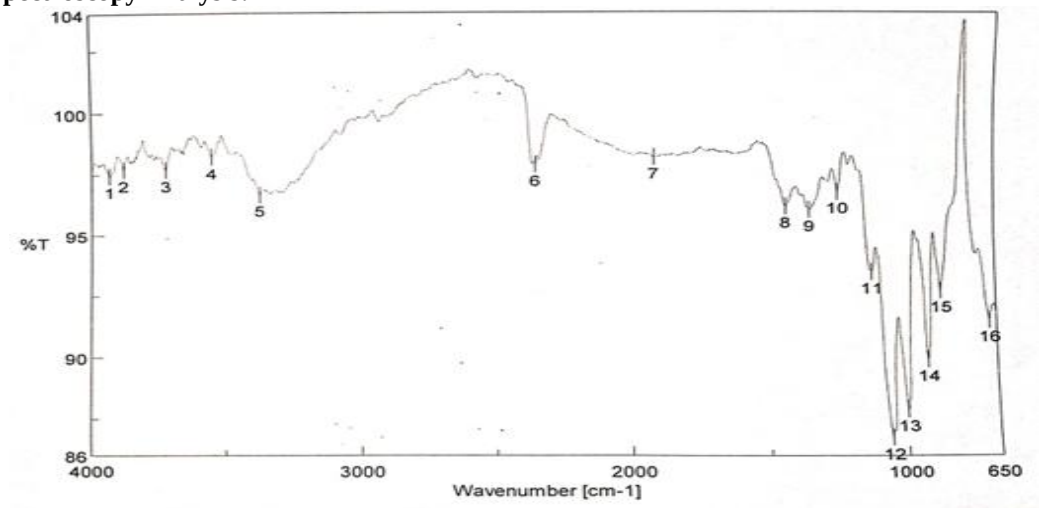

Figure 6: Standard Interferogram

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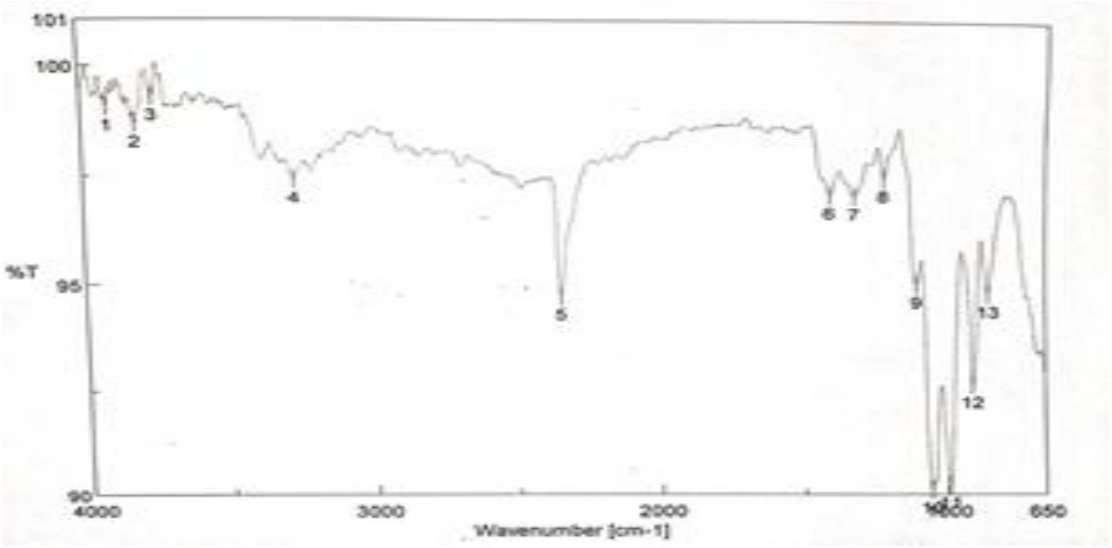

Figure: Sample interferogram

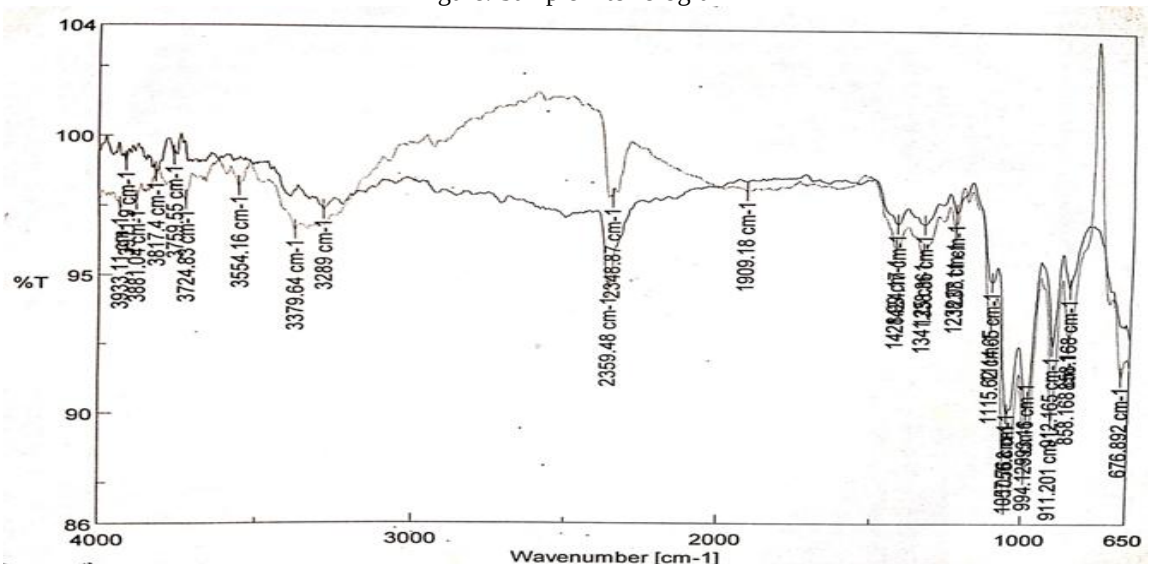

Figure: Overlapping of Standard and Sample

The stability studies were performed for the formulation at 25°C ± 2°C / 60% ± 5% RH, 35°C ± 2°C / 60% ± 5% RH and 40°C ± 2°C / 75% ± 5% RH. The samples were analysed for disintegration time, drug content and drug release. The results indicated that the developed formulation is stable, and did not show any significant difference in drug content, disintegration time and dissolution rate after a study period of three months as shown in table.

IV. DISCUSSION

Traditionally used plant for abortion contains the phytoconstituent Papain, which is a hygroscopic enzyme which gets disintegrated in the gastric environment on oral administration. Present work made an attempt to incorporate this ingredient into an enteric coated tablet, which could be studied further for in vivo abortifacient activity. Molecular docking is performed to evaluate the binding of papain molecule to the endometrial proteins site Lys822. After confirming the positive results of docking score 0.9409 and formulation was designed with enteric-coated tablet containing Papain. Eudragit L100 is well known polymer to be utilized for the purpose. Evaluations resulted positive outcomes with six attempts of formulation. Final formulation was further studied for stability studies for 3 months with acceptable results. Validated UV method was developed for analytical

determination and quantification of Papain in formulated tablets. MCC is used to provide as it has higher protection during stability study phytoconstituent. In vivo studies can confirm the formulation in the future.

V. CONCLUSION

Results of the present work suggest that, traditionally utilised natural abortifacient agents like papain can be formulated using natural enzyme like papain as enteric coated tablet. Evaluation results have shown favourable results and molecular docking is given confirmation about its activity. Further studies may confirm the formulation to be utilized for the benefits of mankind.

SCOPE OF RESEARCH WORK

- Patient compliant formulation.
- Development of stable enzyme containing formulation.
- Less side effects with herbal remedies or formulations.
- Herbal formulation with minimum side effects.

REFERENCES

[1]. Bearak J, Popinchalk A, Ganatra B, Moller A-B, Tunçalp Ö, Beavin C et al. Unintended pregnancy and abortion by income, region, and the legal status of abortion: estimates from a comprehensive model for 1990–2019. Lancet Glob Health. 2020 Sep; 8(9):e1152-e1161. doi: 10.1016/S2214-109X(20)30315-6.

[2]. Ciganda C, Laborde A. Herbal infusions used for induced abortion. J Toxicol Clin Toxicol. 2003;41(3):235-9. doi: 10.1081/clt-120021104. PMID: 12807304.

[3]. Aravind G, Bhowmik D , Duraivel S, Harish G. J Med Plants Stud 2013; 1(1): 7-15

[4]. Carlos ES, Marco TR, Hernandez M, Mirian TP. Phytochemistry 2008; 69: 2263-69. https://doi.org/ 10.101 6/j.phy tochem.2008.05.016

[5]. Singer AJ, Clark RA. N Eng J of Med 1999; 738-46.

[6]. Lohiya NK, Manivannan B, Mishr a PK, Pathak N, Sriram S, Bhande SS et al. Asian J Androl 2000; 4(1): 17-26.

[7]. Poharkar RD, Saraswat RK, Kotkar S. J Herb Med Toxicol 2010; 4(2): 71-75.

[8]. Sheikh F, Krishnamurthy R. J Pharm Sci 2013; 2 (1): 25-34.

[9]. Quintal PC, Flores TG, Buenfil IR, Tintore SG. Indian JMicrobiol 2011; 51(1): 54-60. https://doi.org/ 10.100 7/s12088-011-0086-5

[10]. Keith M. Compression and consolidation of the powdered solids. In: Leon Lachman, Liberman HA, Kanig JL. (eds). Theory and practice of Industrial Pharmacy. ed 3, Mumbai, India: Varghese publishing house, 1991, 66-72.