IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
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Human Journals
**Research Article**
October 2021 Vol.:22, Issue:3


# Research Article on To Investigate, Develop and Evaluate Pharmaceutical Excipient from Orange Peel Powder

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**Submitted:** 23 September 2021
**Accepted:** 29 September 2021
**Published:** 30 October 2021



**Keywords:** Orange peel powder, Perindopril Erbumine (as a modal drug), FTIR

**ABSTRACT**

The present study aimed to investigate, develop and evaluate pharmaceutical excipients from orange peel powder and assess its binding property in tablets by using perindopril erbumine as a modal drug. Now a day's synthetic polymers are mostly used in the pharmaceutical industry they have many disadvantages such as harmful effects on the human body, highly costly but recently natural polymers are used as a pharmaceutical application like orange peel waste material is used as an excipient have many advantages such as nontoxic, nonirritants easily available, it is economically and biocompatible. There are two basic categories of orange: sweet orange and bitter orange. Orange peel consists of several important constituents such as limonene, citral, vitamin c, hesperidin, and pectin are used as pharmaceutical additives. Manufacturing of tablets was done by using direct compression method on lab level tablet press (CEMACH) by direct compression method. Evaluations tests performed on tablets such as Hardness, Weight variation, friability, disintegration test, etc.

## [I]. INTRODUCTION:

Tablet is defined as a compressed solid dosage form containing medicaments with or without excipients. The oral route of drug administration is the most acceptable and frequently used because of the convenience of self-administration, ease of manufacturing, and high degree of dose accuracy. The pharmaceutical industry is focusing on the establishment of novel drug delivery systems rather than investigating and developing new drug entities due to the increased investigational cost of new drugs. The development of sustained drug delivery systems is a challenging task in terms of providing a constant drug release profile retaining the dosage form in the stomach or upper small intestine until all the drug is completely released in the desired time.

An ideal oral drug delivery system will steadily release a measurable and reproducible amount of drug over an extended period. Several mechanisms are involved in the release of drugs from controlled-release formulations such as dissolution-controlled release systems and diffusion-controlled release systems. In dissolution-controlled systems, dissolution is the rate-controlling step.

The goal of any drug delivery system is to make available a therapeutic quantity of drug to the proper site in the body to achieve rapid and then maintain the desired drug concentration.

**Advantages of Sustain-Release Dosage Forms**

1. Decrease in frequency of intakes.

2. Reduce side effects

3. Uniform release of drug over time.

4. Enhanced patient compliance.

**Disadvantages of Sustained Release Dosage forms**

1. Increased cost.

2. Toxicity due to dose dumping.

3. Unpredictable and often poor *in vitro, in vivo* correlation.

4. Risk of side effects or toxicity upon rapid release of contained drug (mechanical failure, chewing or masticating, alcohol intake)

5. Increased potential for first-pass clearance.

6. Need for additional patient education and counseling.

**Objectives of oral sustained released dosage form**

1. To maintain the concentration of drug at a constant level for a preferred period.

2. To reduce the frequency of doses administrated as compared to the conservative dosage form.

3. It should deliver the active entity directly to the site of action, minimizing or eliminating side effects.

4. This may necessitate delivery to specific receptors or localization to cells or definite areas of the body.

5. The safety margin of potent drugs can be improved.

**Factors Affecting Sustained Release Drug Delivery System**

**1. Physicochemical factor**:

Dose size: In general, a single dose that contains a drug of about 500mg-1.0gm is considered the maximum for a conventional dosage form. Compounds which having large dosing sizes can sometimes be given in multiple amounts or formulated into liquid systems. The same criteria also hold for the sustained release dosage form.

**2. Ionization, pka, and aqueous solubility**:

Most drugs are weak acids or bases. While the drugs which are in unchanged form permeate across lipid membranes, therefore pka of the compound and absorptive environment relationship is important. Delivery systems that are dependent on diffusion or dissolution will equally be dependent on the solubility of the drug in aqueous media.

**3. Partition Coefficient:**

To produce a therapeutic effect in another area of the body, when a drug is administered to the GI tract, it must cross a variety of biological membranes. It is common to consider that these membranes are lipidic; therefore the partition coefficient of oil-soluble drugs is important in determining the effectiveness of membrane barrier penetration.

**4. Biological factor**

1. Half-life

2. Therapeutic index

3. Absorption window

4. Plasma concentration-response relationship

5. Concentration dependency on the transfer of drugs.

**Drug:**

**Perindopril Erbumine**

Hypertension is defined as an increased blood pressure 140/90 mmHg. Hypertension is a risk factor for myocardial infarction, stroke, congestive heart failure, end-stage renal disease, and peripheral vascular disease. The World Health Organization reported that suboptimal blood pressure (SBP > 115 mmHg) is responsible for 62% of all cerebrovascular diseases and 49% of all ischemic heart diseases. In addition, suboptimal blood pressure is the number one cause of death throughout the Western world.

**Antihypertensive agents**

Antihypertensive agents are the drugs that lower blood pressure in hypertensive patients.

**Hypertension**

Hypertension is defined as an increased blood pressure 140/90 mmHg.

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cerebrovascular diseases and 49% of all ischemic heart diseases. In addition, suboptimal blood pressure is the number one cause of death throughout the Western world.

**Classification of anti-hypertensives**

1. Diuretics

e.g. Chlorthalidone, Clopamide, Indapamide

2. β Adrenergic blockers

e.g. Acebutolol, Atenolol, Metoprolol, Propranolol, Timolol

3. α Adrenergic blockers

4. e.g. Terazosin, Prazosin, Doxazosin

5. α + β Adrenergic blockers

6. e.g. Labetalol, Carvedilol

7. ACE inhibitors

e.g. Perindopril, Captopril, Enalapril, Lisinopril, Fosinopril, Trandolapril, Benazepril etc.

8. Calcium channel blockers

e.g. Amlodipine, Felodipine, Nifedipine, Nimodipine, Verapamil

9. Vasodilators

e.g. Hydralazine, Minoxidil, Sodium nitroprusside

10. Angiotensin-II receptor antagonists

e.g. Candesartan, Losartan, Valsartan

11. Central sympatholytics

e.g. Clonidine, Methyldopa

**Clinical classification of hypertension**

Although hypertension is a rise in blood pressure above the normal clinical values, which can be mild to malignant and therefore classified clinically as summarized below.

**Table No.1.1**

| Category | Systolic (mm Hg) | Diastolic (mm Hg) |
|---|---|---|
| Normal | >130 | <85 |
| High Normal | 130-139 | 85-89 |
| **Hypertension** | | |
| Mild stage(stage1) | 140-159 | 90-99 |
| Moderate(stage2) | 160-179 | 100-109 |
| Severe(stage3) | 180-209 | 110-119 |
| Very sever(stage4) | >210 | >120 |
| Malignant hypertension | >200 | >140 |

**An overview on Perindopril Erbumine**

Numerous studies demonstrated the efficacy of perindopril in the therapy of essential hypertension. Perindopril doses of 4 to 16 mg administered once daily are more effective than placebo in the treatment of mild-to-moderate hypertension. Doses greater than 8 mg offer no advantage in most patients; however, in some patients doses, 12 or 16 mg daily provide greater therapeutic benefit.

**Orange**

Oranges are important medicinal plants of the family *Rutaceae*. It is reported that their pulp, as well as peel, have antibacterial potential in addition to other properties. The synthetic polymers used as excipients have many disadvantages such as high cost, toxicity, nonbiodegradability, and environmental pollution caused during their synthesis. Natural polymer like pectin is easy to isolate and purify, it is non-toxic and biocompatible. Pectin has been used in the food industry but recently they are being explored for its other pharmaceutical applications such as binding, thickening, suspending properties. Pectin, a multifunctional constituent contained in the cell wall of terrestrial plants. Pectin is a non-starch linear polysaccharide consisting of 1, 4 D-galacturonic acids. Galacturonic acid of

pectin may or may not be esterified with methanol or acetic acid, in which case percentage esterified groups are expressed as the degree of methoxylation (DM) and degree of acetylation (DA) respectively.

**Characteristics**

It is a small tree with a smooth, greyish brown bark and branches that spread into a regular hemisphere. The leaves are oval, alternate, evergreen, size ranging from 3 to 4 inches long, rarely with a spine in the axil. They are glossy, dark green on the upper surface, and lighter beneath. The calyx is cup-shaped and the thick, fleshy petals, five in number, are intensely white and curl back. The fruit is earth-shaped, a little rougher and darker than the common, sweet orange: the flowers are more strongly scented, and the glands in the rind are concave instead of convex. The dried peel is brittle and hard, dark orange-red, the surface is rough with oil glands that are slightly raised. The inner surface is yellowish-white with pithy on them.

**Table No.1.2 Chemical constituent of orange peel as following**

| Sr No | Name of Chemicals | Concentration (%) | Therapeutic Uses |
|---|---|---|---|
| 1 | Limonene | 90% | Insecticides |
| 2 | Citral | 4% | Skin carcinogenesis |
| 3 | Vitamin C | — | Supplement |
| 4 | Pectin | — | Additives |
| 5 | Hesperidin | — | Bioflavonoid |
| 6 | Aurantimaric acid | — | Bitter tonic |

**Botanical classification of Orange kingdom planate**

Division: Magnoliophyta

Class: Dicotyledons

Sub Class: Sapindales

Order: Rosidae

Family: Rutaceae

Subfamily: Aurantoideae

Genera: Citrus

Sub genera: Papeda

**Fig.No.1.1. Orange pill**

**Fig.No.1.2. *Citrus aurantiamarin***

**Health Benefits of Orange peel**

The orange peel provides these health benefits:

1. **Healthy skin**

Orange peels are loaded with antioxidants and vitamin E. So applying peels on the skin directly helps to clear inflammatory conditions and also prevents age spots and wrinkles. The high presence of Vitamin C lowers the appearance of marks and spots which are caused by premature aging. Orange peel extracts help to clear spots caused by burns, exposure, and toxins. It is helpful for pimples, blackheads, and acne as it cleanses pores deeply.

2. **Treat allergies**

Orange peels have active compounds which provide a regulatory effect on the immune system. It suppresses allergic reactions and lowers strain on the body's defenses.

3. **Healthy cholesterol levels**

Orange peels have great amounts of fiber and different nutrients so when consumed; it promotes cardiovascular health by preventing cholesterol build-up and lowering blood pressure. Orange peels contain flavonoids and phytochemicals which acts as a natural aid for people having uncontrolled cholesterol. Antioxidants help to clear arteries and prevent plaque formation which causes blood clots and blockages. It is helpful to maintain cardiovascular health. It lowers the chances of hypertension, strokes, and heart attacks.

4. **Cure for asthma**

The consumption of orange peel extract in powdered form or tea can soothe inflammation in respiratory tracts.

5. **Digestive health**

Peels contain fiber that stimulates bowel function and also prevents constipation. Daily consumption promotes bowel movements and also promotes the elimination of waste in the colon. It prevents diarrhea, irritable bowel syndrome, and inflammatory diseases.

6. **Traditional uses**

Make a face pack with 2 tbsp of yogurt and 1 tbsp of orange peel powder. Apply it to the face and wash after 20 minutes to get fresh, clear, and toned up tight-looking skin.

Make a paste with 1 tbsp. of an orange powder, 1 tbsp. sandalwood powder, 1. tbsp of walnut powder, 2 tbsp of rose water, and 2 to 3 drops of lemon juice. Apply it to the face for five minutes and wash it. It is an exfoliator.

With 1 tbsp of Multani mitti and 1 tbsp of orange peel powder, make a paste by adding rose water. Apply it to the neck and face and wash it when it becomes semi-dry. It helps to cleanse skin deeply and also pull out whiteheads and blackheads.

To brighten skin, make a smooth paste by adding a few drops of lime, 2 tbsp. orange peel powder, a tablespoon of each sandalwood powder, and fuller's earth. Apply it to the face and after 30 minutes, rinse off.

Use tea with an extract of orange peel to get soothing lung relief and decongestion.

Make an air freshener by adding peels in boiling water. Inhale the steam or air to provide relief from headaches.

Use orange peel teas internally to stimulate appetite and help with stomach cramps.

7. Orange peels are helpful for respiratory problems and allergies.

## [II]. MATERIALS AND METHODS:

### List of materials

A list of materials and equipment was used for the formulation and evaluation given in tables.

**Table No.2.1 Materials Used**

| Sr.no. | Material | Source |
|---|---|---|
| 1 | Perindopril Erbumine | Aurobindo Pharma Limited, Hyderabad |
| 2 | HPMCK100M | S.d. Fine chemicals Chemicals, Mumbai |
| 3 | MCC | S.d. Fine chemicals limited, Mumbai |
| 4 | Orange peel powder | Latur market |
| 5 | Talc | S.d. Fine chemicals limited, Mumbai |
| 6 | Magnesium stearate | S.d. Fine chemicals limited, Mumbai |

**Table No.2.2 Types of equipment used**

| S. No | Name of the Equipment | Supplier / Manufacturer |
|---|---|---|
| 1. | Electronic balance | Shimadzu BL-2204 |
| 2. | Hot air oven | Spencers |
| 3. | Tablet compression machine | Rimek Minipress-II MT, Karnavati Ltd |
| 4. | Disintegration apparatus | Campbell electronics, Mumbai. |
| 5. | Friability test apparatus | Roche Friabilator. |
| 6. | Hardness tester | Monsanto hardess tester |
| 7. | FTIR Spectrophotometer | Perkin Elmer IR Series Model no.-21 Spectrometer |

**PRE-FORMULATION STUDIES:**

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

**The following pre-formulation studies were performed.**

Study of organoleptic properties

Solubility analysis

Drug powder characterization

Drug-excipients compatibility study by FT-IR

**Organoleptic properties**

The Organoleptic character of the drug-like color, odour, taste, and appearance plays an important role in the identification of the sample and hence they should be recorded in descriptive terminology.

**Solubility studies**

It is important to know about the solubility characteristics of a drug in aqueous systems since they must possess some limited aqueous solubility to elicit a therapeutic response. Quantitative determination of solubility was made by preparing a saturated solution of the drug in a constant volume of water, methanol, ethanol, acetic acid, and ethyl acetate and the resulting solutions were kept at room temperature for 24 hours with intermediate shaking.

**Drug powder characterization**

**Angle of repose**

The equation for calculating the angle of repose is tan-1(2h/d). Using your scientific calculator, multiply the height by 2 and divide this value by the distance. Then, hit the inverse tan key (or tan-1) and the answer is just calculated.

**Method**

The angle of repose was determined by using the funnel method. The height of the funnel was adjusted in such a way that the tip of the funnel just touches the heap of the blends. The accurately weighed blend was allowed to pass through the funnel freely on the surface. The height and diameter of the powder cone were measured and the angle of repose was calculated using the following equation.

$$\Theta = \tan\text{-}1\ (h/r)$$

Where, h = height of heap, r = radius of the heap, Θ = angle of repose.

**Table No.2.3 Selected excipients used in formulations**

| Sr.NO | EXCIPIENT USED | FUNCTION |
|---|---|---|
| 1 | Starch | Disintegrant |
| 2 | Methyl cellulose | Binder |
| 3 | Lactose | Diluent |
| 5 | Talc | Glidant |
| 6 | Amaranth | Colouring agent |

**Bulk density**

Bulk density is defined as the mass of the powder divided by the bulk volume. Bulk density largely depends on particle shape as the particle becomes more spherical, bulk density increases. In addition, as the granule size increases bulk density decreases.

It is the ratio between a given mass of a powder and its bulk volume

Bulk Density = Bulk Mass / Bulk Volume

**Method**

A given quantity of the power was transferred to a measuring cylinder and tapped mechanically either manually or using some tapping device till a constant volume is obtained. This volume is the bulk volume (v) and it includes the true volume of the powder and the void space among the powder particles. A given peak of powder has air spaces between the particles. This air space is called void space or void volume.

**Tapped density**

It is the ratio of the total mass of the powder to the tapped volume of powder. The volume was measured by tapping the powder. Then the tapping was done and the tapped volume was noted. The tapped density was calculated by using the following formulae:

$$\text{Tapped Density} = \frac{m}{Vf}$$

Where, m = initial weight of material in gm,

*Vf*= volume of material after tapping.

**Measurement of powder compressibility**

The compressibility Index and Hauser's ratio are measures of the propensity of a powder to be compressed. As such, they are measures of the relative importance of inter particulate interactions. In a free-flowing powder, bulk density and tapped density have closer values as such interactions are generally less. For poorer flowing materials, there are frequently greater antiparticle interactions, and hence, a greater difference between bulk and tapped densities was observed. These differences are reflected in the compressibility Index and Hauser's ratio calculated by the formula.

$$\text{Compressibility index: } = \frac{100\ (V0\ Vf)}{V0}$$

Where, Vf= final tapped volume,

V0 = initial untapped volume

$$\textbf{Hauser's ratio} = \frac{V0}{Vf}$$

Where, Vf = final tapped volume, Vo = initial untapped volume.

**Drug-Excipients Compatibility Studies:**

**Fourier Transform Infrared (FTIR) Spectroscopy**

FT-IR spectra of pure drug, Pure HPMC K100 M, Pure Xanthan Gum & physical mixtures of this polymer with the drug were recorded on Bruker alpha FT-IR spectrophotometer using KBr discs. The instrument was operated under dry air purge and the scans were collected at scanning speed 2 mm/sec with a resolution of 4 cm-1 over the region 4000-400 cm-1. The scans were evaluated for the presence of principle peaks of the drug, shifting and masking of drug peaks and appearance of new peaks due to polymer interaction.

**Formulation of sustained-release tablets of Perindopril Erbumine by direct compression method**

The key ingredients included in the formulation are Hydrophilic polymers: Talc and HPMC K100M

Diluent: MCC

Glidant: Talc

Lubricant: Magnesium Stearate

Binder: Orange peel powder

Accurately weighed quantities of polymer and MCC were taken in a mortar and mixed geometrically to this required quantity of Perindopril Erbumine was added and mixed with the help of pestle. The powder blend was then lubricated with magnesium stearate and talc mixed for about 3minutes. Compression operation was carried on rotary tablet compression machine fitted with 6 mm round-shaped, standard flat face punch sets having plain on both sides at average weight 100 mg/tab.

Before going to compression powder blend was evaluated for all physical parameters like angle of repose, bulk density, tapped density, carr's index, Hausner's ratio.

**The formula of sustained-release tablets of Perindopril Erbumine**

**Table No.2.4 Formulation of Perindopril Erbumine tablet**

| Ingredients (mg) | F1 | F2 | F3 | F4 | F5 | F6 |
|---|---|---|---|---|---|---|
| Perindopril Erbumine | 4 | 4 | 4 | 4 | 4 | 4 |
| HPMC K100M | 30 | 30 | 30 | 30 | 30 | 30 |
| Orange peel | 2 | 4 | 6 | 8 | 10 | 12 |
| MCC | 111.5 | 109.5 | 107.5 | 105.5 | 103.5 | 101.5 |
| Talc | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 |
| Mg. stearate | 1 | 1 | 1 | 1 | 1 | 1 |
| Total wt(mg) | 150 | 150 | 150 | 150 | 150 | 150 |

**Evaluation of prepared tablets of Perindopril Erbumine**

**Tablet thickness and diameter**

The thickness and diameter of tablets were important for the uniformity of tablet size. Thickness and diameter were measured using vernier calipers.

**Hardness**

This test is used to check the hardness of a tablet that may undergo chipping or breakage during storage, transportation, and handling. In these six tablets were selected at random and the hardness of each tablet is measured with Monsanto hardness tester. The hardness is usually measured in terms of $kg/cm^2$.

**Friability**

The friability test was carried out to evaluate the hardness and stability instantly in Roche Friabilator. Here twenty tablets were weighed (Wo) initially and put in a tumbling and rotating apparatus drum. Then, they are subjected to fall from 6 inches in height. After completion of 100 rotations i.e., 25 rpm for 4 minutes, the tablets were again weighed (w). The percent loss in weight or friability (F) is calculated by the formula:

F= (1-W/Wo) x 100

**Weight variation**

This test is performed to maintain the uniformity of weight of each tablet which should be in the prescribed range. This was done by sampling randomly and weighing 20 tablets and the average weight was calculated. Not more than two of the individual weights deviate from the average weight by more than the percentage shown in the table 8 and none deviate by more than twice the percentage The mean and standard deviation were determined.

**Table No.2.5 Pharmacopoeial specifications for tablet weight variation**

| **Average weight of tablets (mg) (I.P)** | **Average weight of tablets (mg) (U.S.P)** | **% deviation allowed** |
|---|---|---|
| Less than 80 | Less than 130 | 10 |
| 80 – 250 | 130 – 323 | 7.5 |
| More than 250 | More than 324 | 5 |

**Content uniformity**

This test was performed to maintain the uniformity of weight of active ingredient in each tablet which should be in the prescribed range according to the Indian Pharmacopoeia. This test was performed by taking twenty tablets randomly, weighed and powdering. A quantity of powdered tablet equal to 100 mg of perindopril Erbumine is dissolved in 0.1 N HCL in a 100ml volumetric flask. It is diluted and the absorbance is measured at 224 nm using 0.1 N HCL as blank and the % drug content was estimated using the following formula.

Absorbance-intercept Concentration (mcg/ ml) = ----------

Slope

Drug content (mg) = concentration x dilution factor

Drug content (mg)

% Drug content= 100

Label claim (mg)

**Stability protocol**

The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity and light and to establish a retesting for the drug substances or a shelf-life for the drug product and recommended storage conditions.

The storage conditions used for stability studies were accelerated conditions (40°C±2°C/75%±5% RH). A stability study was carried out for the optimized formulation. Tablets of optimized formulation were packed in strips and kept in a stability chamber for 3 months on above mention temperature.

The samples were kept at 40°C±2°C/75%±5% RH and analyzed for weight variation, hardness, friability.

**[III]. OBSERVATIONS AND RESULTS:**

**Pre-formulation Studies:**

**Appearance**

The sample of Perindopril Erbumine was white or almost white, odourless or almost odourless crystalline powder.

**Solubility**

The Perindopril Erbumine was soluble in water, methanol, ethanol, acetic acid and ethyl acetate, very slightly soluble in ether, chloroform and benzene.

**Melting point**

The melting point was found to be 126-128ºC.

**Physical characteristics of Orange peel powder**

**Table No 3.1: Physical characteristics of orange peel powder.**

| S. No | Parameter | Specifications |
|---|---|---|
| 1 | Bulk density (g/ml) | 0.610 |
| 2 | Tapped Density (g/ml) | 0.501 |
| 3 | Hausner's ratio | 1.12 |
| 4 | Compressibility index (%) | <16 |
| 5 | Angle of repose | 27.07 º |

All the powder characteristics were good and satisfied according to pharmacopeia.

**FTIR Studies**

Potential chemical interactions between the drug and polymer may change the therapeutic efficacy of the drug. To investigate the possibilities of chemical interaction between drug and excipients. FTIR spectra of pure drug and optimized formulations were analyzed over the range 400-4000cm-1. Compatibility studies were performed using FT-IR Spectrophotometer. The FT-IR spectrum of pure Perindopril Erbumine drug was compared with FT-IR spectrum of physical mixture of Perindopril Erbumine (Perindopril Erbumine, HPMC K100, Orange peel powder, MCC, Talc and Mg. stearate. The spectra for all formulations are shown below Fig no 3.1 to Fig no 3.7.

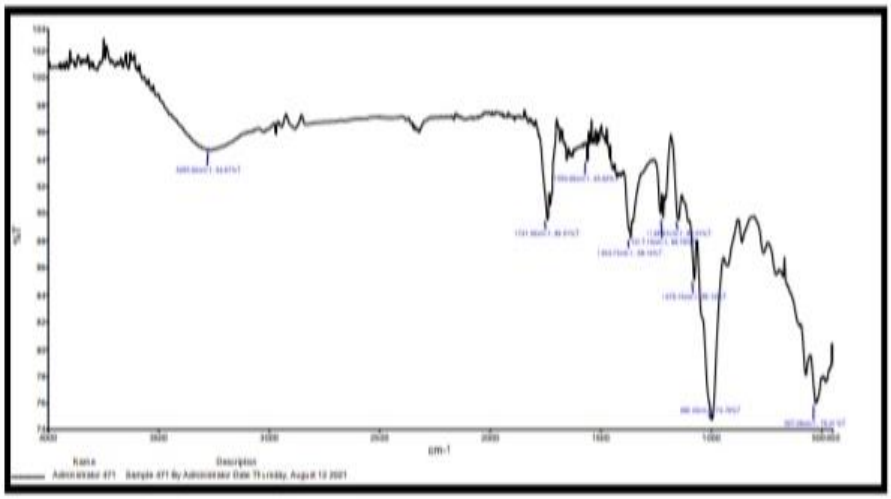

**Fig. No 3.1 FTIR Spectra of Perindopril Erbumine**

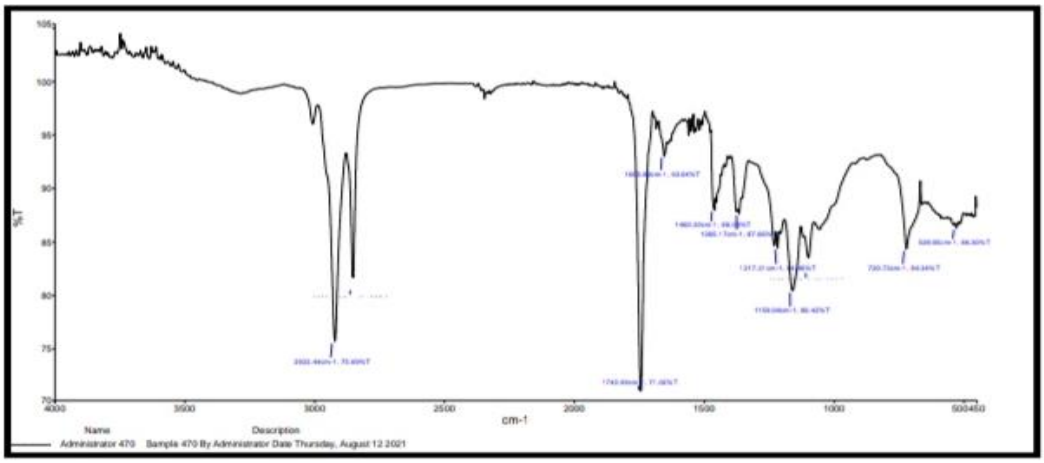

**Fig. No. 3.2 FTIR Spectra of HPMC**

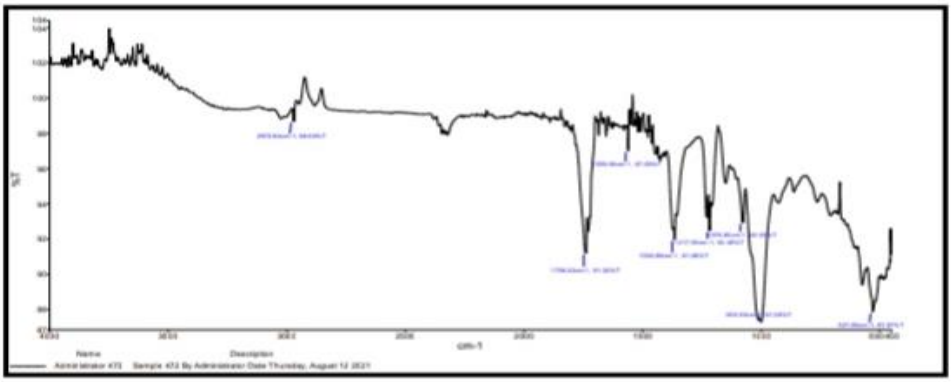



**Fig. No. 3.3 FTIR Spectra of Talc**

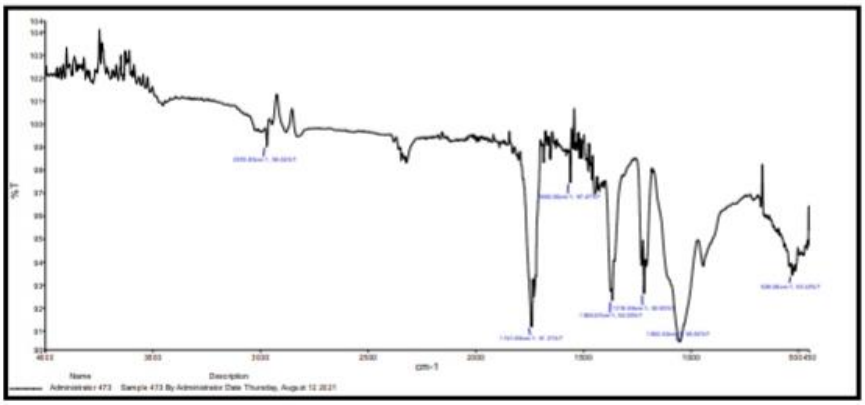

**Fig. No. 3.4 FTIR Spectra of MCC**

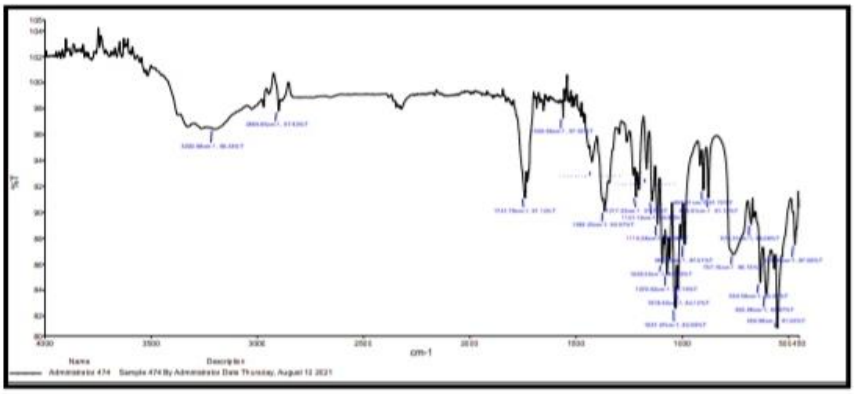

**Fig. No.3.5 FTIR Spectra of Mg. stearate**

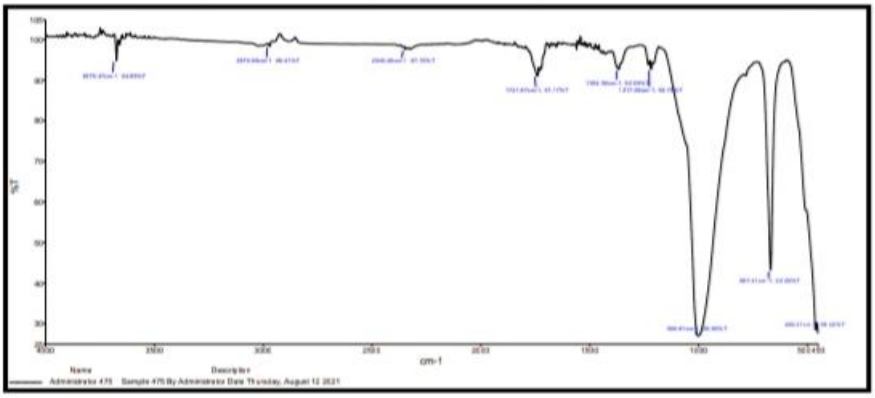

**Fig. No. 3.6 FTIR Spectra of Orange peel powder**

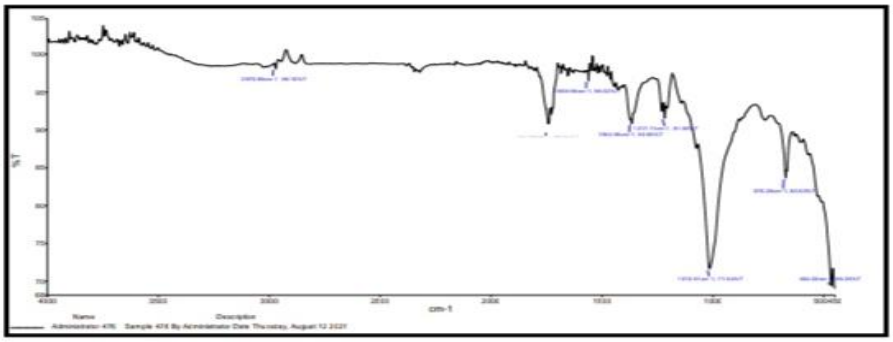

**Fig. No. 3.7 FTIR Spectra of Drug + Excipient**

**Table No 3.2: FT-IR Peaks of various compounds**

| Functional groups | Standard Frequency | Observed peak |
|---|---|---|
| O-H Stretching | 3200-3600 | 3675.81 |
| C-H Stretching | 2850-3600 | 2915.78 |
| C-H Stretching | 2850-3000 | 2849.54 |
| C=O Stretching | 1670-1820 | 1738.27 |
| N-O Stretching | 1515-1560 | 1577.83 |
| -C-H Bending | 1350-1480 | 1447.11 |
| -C-H Bending | 1350-1480 | 1365.15 |
| C-N Stretching | 1080-1360 | 1229.01 |
| C-N Stretching | 1080-1360 | 1217.07 |
| C-I Stretching | 500 | 463.54 |

FTIR spectrum analysis showed that there is no appearance or disappearance of any characteristic peaks of pure perindopril erbumine and in the physical mixture of drug with polymer and excipients. The presence of peaks at the expected range confirms that the materials taken for the study are genuine. The results were shown in table no Due to stretching C-N, C-NH2, C=O, C-CH3 and N-H respectively in optimized formulations also these peaks were well preserved with additional peaks which correspond to the excipients used in the formulation. This indicated that no drug excipients interaction.

**Evaluation of pre-compression parameter**

**Table No. 3.3 Powder characterization of formulation**

| Formulation code | Angle of repose (± SD) | BD (gm/ml) (± SD) | TD (gm/ml) (± SD) | Carr's index (%) (±SD) | Hausner's ratio (± SD) |
|---|---|---|---|---|---|
| **F1** | 23.05±0.04 | 0.602±0.02 | 0.505±0.02 | 15.81±0.05 | 1.03±0.05 |
| **F2** | 25.11±0.01 | 0.606±0.03 | 0.507±0.01 | 15.96±0.07 | 1.08±0.04 |
| **F3** | 25.81±0.04 | 0.610±0.06 | 0.501±0.01 | 16.10±0.04 | 1.13±0.02 |
| **F4** | 27.09±0.07 | 0.614±0.04 | 0.504±0.07 | 16.05±0.01 | 1.16±0.06 |
| **F5** | 27.04±0.09 | 0.598±0.03 | 0.511±0.03 | 16.09±0.03 | 1.19±0.03 |
| **F6** | 26.81±0.06 | 0.609±0.01 | 0.516±0.01 | 16.15±0.01 | 1.18±0.01 |

(n=3±S.D) (S.D=Standard deviation)

For the powder blend of all the formulated batches, the angle of repose was found to be in the range of 23° to 27°, thus indicating that the flow properties were excellent. Hausner's ratio was less than 1.03 for all the batches indicating good flow properties.

**Evaluation of Perindopril Erbumine tablets**

**Table No. 3.4 Evaluation of prepared tablet**

| Formulation code | Weight variation( mg) (±SD) | Hardness (kg/cm2) (±SD) | Thickness (mm) (± SD) | Drug content (mg) (± SD) | Friability % |
|---|---|---|---|---|---|
| F1 | 150.4±1.24 | 4.30±0.23 | 3.007±0.02 | 143.60±0.19 | 0.40 |
| F2 | 150.8±1.61 | 4.25±0.30 | 3.008±0.02 | 147.12±0.27 | 0.51 |
| F3 | 150.9±1.56 | 3.50±0.11 | 3.001±0.02 | 141.87±0.41 | 0.60 |
| F4 | 150.1±1.28 | 3.90±0.23 | 3.011±0.02 | 148.28±0.33 | 0.64 |
| F5 | 150 ±1.16 | 4.10±0.15 | 3.009±0.02 | 142.90±0.26 | 0.48 |
| F6 | 149.6±1.42 | 4.05±0.2 | 3.010±0.0 | 144.76±0.17 | 0.43 |

(n=3±S.D) (S.D=Standard deviation

The histograms of hardness, thickness, weight variation, friability and drug content were mentioned in the above figure.

The weight variations for all the formulations F1 to F6 were within the pharmacopeia specification.

The thickness of all the formulations F1 to F6 was in the range of 3.001-3.011 mm.

The hardness of all the formulations F1toF6 was in the range of 3.50-4.30 kg/cm$^2$.

Friability of all the formulations F1 to F6 was in the range of 0.40.64%.

Drug content all the formulations F1 to F6 was in the range of 93to 100%.

All the prepared formulations were tested for physical parameters like Hardness, Thickness, Weight variation, Friability, which were found to be within pharmacopoeial limits. The drug content of all the formulations was determined and was found to be within the permissible limit. This study indicated that prepared formulations were good.

**Table No. 3.5: Organoleptic properties of prepared tablets**

| Formulation Code | Color | Odour | Shape of tablet |
|---|---|---|---|
| **F1** | White colour | odourless | Concave, round and flat |
| **F2** | White Colour | odourless | Concave, round and flat |
| **F3** | White Colour | odourless | Concave, round and flat |
| **F4** | White colour | odourless | Concave, round and flat |
| **F5** | White Colour | odourless | Concave, round and flat |
| **F6** | White Colour | odourless | Concave, round and flat |

**Accelerated Stability Studies**

In any rational design and evaluation of dosage forms for drugs, the stability of the active component must be major criterion in determining their acceptance or rejection. In the present study, stability studies were carried out on formulation F4.The tablets were stored at 40 ± 20C and 75 ± 5 % RH for a duration of 1 months and analyzed for their physical

parameters, hardness, drug content and friability after 1A month the data were shown in table no 3.6.

**Table No.3.6 Accelerated Stability Studies**

| Parameter | Initial | After one month |
|---|---|---|
| Shape | Round and Flat | No Change |
| Colour | White | No Change |
| Hardness | 4.0 | No Change |
| Friability (%W/W) | 0.58 | No Change |
| Drug Content | 148.22 | No Change |

## [IV]. CONCLUSION

In the present study, six different concentrations of orange peel powder-based tablets were prepared by direct compression method. The powder of orange peel was found to have very good flow properties and was further used for tablet formulation. The formulation of tablet prepared was found to pass all evaluation parameters including weight variation, friability, hardness, thickness showing that the orange peel can be successfully used in the preparation of matrix formulation. The orange peel powder exhibited good binding properties for the perindopril erbumine tablet and suspension. The increased concentration of orange peel powder showed small retardation in drug release from tablet and suspension. Therefore, orange peel pectin powder can be used as a pharmaceutical excipient in tablet and suspension preparation. Orange peel pectin powder was optimized as a binding agent respectively.

**The following conclusions can be drawn from the result obtained.**

The preformulation parameters like organoleptic properties, angle of repose, bulk density, tapped density, Hausner's ratio, carr's index, and compressibility index of the pure drug were evaluated and complied with the pharmacopeia specifications.

FTIR studies showed that there was no interaction between drug and polymer.

Sustained-release tablets of perindopril erbumine were formulated by using polymers like HPMC K100 M and Microcrystalline cellulose.

The formulated batches were evaluated for physicochemical parameters and dissolution profiles. The physical properties like hardness, weight variation, and friability of the majority

of the batches complied with the pharmacopoeial specifications. The drug content of all tablets was in the range of 93 – 100%.

The accelerated stability studies were carried out for F5 formulation for 1 month. Data revealed that there was no considerable difference.

The above study concluded that F5 was the optimized formulation that has shown better results. However further *in vivo* studies can be carried out to support the results.

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