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Original Article

Development And In Vitro Evaluation of Tablet in Capsule Drug Delivery System for Simultaneous Administration of Ibuprofen and Omeprazole

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ABSTRACT

The study focuses on the development and in vitro evaluation of a tablet-in-capsule drug delivery system for the simultaneous administration of ibuprofen and omeprazole. The formulation of ibuprofen tablets was carried out using hydroxyl propyl cellulose and ethyl cellulose, which were blended, compacted, and compressed to form tablets with specific hardness, thickness, and weight. For omeprazole, barrier and enteric coatings were applied to the drug-loaded pills to ensure proper release characteristics. The tablet-in-capsule approach involved selecting a suitable capsule size to accommodate the enteric-coated ibuprofen and immediate-release omeprazole. Preformulation studies, including bulk density, Carr's index, and angle of repose, were conducted to assess the flow properties of the drug blends. Evaluation of the combined capsule formulations showed that F1 exhibited the best in vitro drug release profile, with 90% of the ibuprofen and omeprazole released within 30 minutes. The results indicated that the formulation F1 is optimal in terms of drug release, disintegration time, and overall drug content uniformity.

Keywords: Ibuprofen, Omeprazole, Tablet-in-Capsule, Drug Delivery System, In Vitro Evaluation, Disintegration, Drug Release, Preformulation Studies, Enteric Coating, Combined Capsule

INTRODUCTION

Ibuprofen is a widely used analgesic and anti-inflammatory drug, while omeprazole is a proton pump inhibitor commonly used to treat gastric acid-related disorders. The concurrent administration of these drugs is often required for patients with conditions such as gastric ulcers or pain associated with inflammatory disorders. However, their simultaneous use in a single dosage form presents challenges in terms of optimizing drug release profiles. This study aims to develop and evaluate a tablet-in-capsule drug delivery system for the simultaneous administration of ibuprofen and omeprazole, providing a convenient and effective solution for combination therapy. The main objective is to formulate a system that ensures optimal drug release, minimizes drug interactions, and improves patient compliance.

2. Drug Profile:

2.1 Ibuprofen:

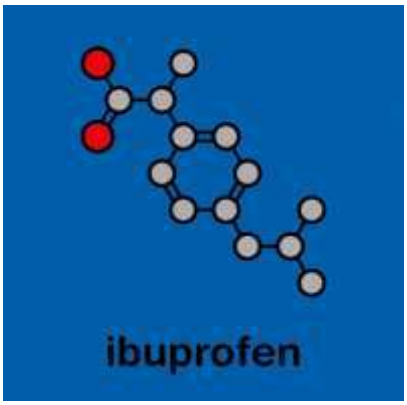

Fig: 1 Structure of Ibuprofen

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

- ✓ **IUPAC Name**: 2[4-(2-methylpropyl) phenyl] propionic acid**.**
- ✓ **Molecular Weight**: 206.29g/mol
- ✓ **Molecular Formula**: $C_{13}H_{18}O_2$
- ✓ **MOA**: Reversibly (cox-1andcox-2) propionic acid.
- ✓ **Appearance:** White crystalline powder.
- ✓ **Odour:** Characteristic odour.
- ✓ **Solubility:** Soluble in ethanol, Chloroform & Acetone and Insoluble in water.
- ✓ **Routes:** Oral, Rectal and topical intravenous
- ✓ **Bioavailability:** 49-73%.
- ✓ **Protein binding:** 92-99%.
- ✓ **Metabolism:** Hepatic (CYT2CS).
- ✓ **Half-life:** 1-4 hrs.
- ✓ **Excretion:** 48% Renal.
- ✓ **Storage:** To be stored at room temperature.
- ✓ **Medicinal Uses:** Analgesic, Antipyretic and for symptomatic relief of dysmenorrheal, Rheumatoid arthritis and oesteroarthritis, Rheumatic and non-rheumatic inflammatory disorder.
- ✓ **Side Effects:** Nausea, vomiting, dyspepsia, heart burn, diarrhoea, fluid retention, tinnitus, oedema, severe GI bleeding, ulceration, perforation, dizziness, skin irritation, anemia, apnea, respiratory infection, sepis and epigastritis**.**
- ✓ **Contraindication:** Active peptic ulcer, Hypersensitivity, Asthma, Renal or Hepatic disorder.
- ✓ **Drug-Drug Interactions:** Notable drug-drug interactions with the pharmacokinetics of ibuprofen include enhanced effect with monoclobemide, Increased risk of GI bleeding with warfarin, Reduces anti-platelet effect of aspirin, Increased risk of methotrexate and lithium toxicity.

2.2 Omeprazole:

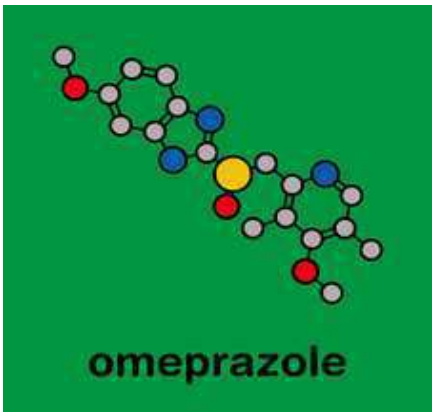

Fig: 2 Structure Of Omeprazole

- ✓ **Molecular weight:** 345.42
- ✓ **Molecular formula**: $C_{17}H_{19}N_3O_5$
- ✓ **Colour:** white crystalline powder.
- ✓ **Solubility**: freely soluble in ethanol methanol, slightly soluble in acetone, very slight soluble in water.
- ✓ **Temperature:** 155°C
- ✓ **Half-life:** 0.5-1 hour
- ✓ **Pharmacokinetics:** The acidic pH in the parietal cell acid canaliculated is required for drug activation and since food stimulation acid production these drug's ideal should be given in 30 min before meals.
- ✓ **Side effect:** Nausea, abdominal pain, constipation, diarrhea, head ache, skin rashes

- ✓ **Storage:** well-closed, light resistance container a cool & dry place.

- ✓ **Mechanism of action:** Omeprazole belong to a new class of antisecretory compound the substituted benzimidazole, that do not exhibit ant cholinergic or H2 histamine antagonistic properties, but that suppress gastric acid secretion by specific inhibition of the H/K ATPase enzyme system at the secretary surface of the acid (proton) pump within the gastric mucosa, omeprazole has been characterized as a gastric acid-pump inhibitor, in that it blocks the final step of acid production. This effect is dose-related and leads to inhibition of both basal and stimulated acid secretion irrespective of the stimulus. Animal studies indicate that after rapid disappearance from plasma, omeprazole can be found within the gastric mucosa for a day or more.

- ✓ **Uses:** proton pump inhibitor, gastric duodenal ulcer, H2 receptor antagonist.

MATERIAL AND METHODS:

3.1 Formulation of Ibuprofen Tablet:

The composition of different formulations of ibuprofen tablets along with hydroxyl propyl cellulose and ethyl cellulose were weighed accurately and pass throw 44 # and mixed thoroughly. Then mixture blended for 13 min at 20 rpm by using V-blender og 100 lit. obtained blend is passed through roll compactor for compaction at varying auger rpm (6 to 7, 10 to 11, 14 to 15, 18 to 19, 23 to 24, 27 to 28). These obtained compacts were passed through multi mill for milling which gives granules. Granules are mixed with magnesium stearate to improve its flow properties, then compressed on a 24-punch tablet machine cadmach-16 multi stage punching machine). The tablets were round and flat with an average diameter of 10.0 ± 0.1 mm and a thickness of 4.1 ±0.2mm.

3.2 Formulation of Omeprazole Pills:

Barrier Coating: 500ml of purified water is taken beaker and kept for stirring under a mechanical stirrer specified quantities of HPMC light magnesium carbonate and mannitol were add slowly to form a uniform suspension, drug loaded pills were coated with the above suspension using fluidesed bed coaters (FBC). Dried pills collected and coating efficiency was calculated.

Enteric Coating Stages: 300ml of isopropyl and 900ml of acetone were taken in abeaker and kept for stirring under the mechanical stirrier. Specified quantity of enteric coating polymers plastizers (Eudrajit L-100, tri ethyl citrate (or) HPMC diethyl phthalate cetyl alchol) titanium dioxide (previously passed through 200 ach) were added slowly to form a uniform suspension. Stirring was continoused for 30 min. barrier coated pills were coated above suspension using fluidesed bed coaters (FBC). Dried pills collected and coating efficiency was calculated.

Preparation Of Tablet In Capsule Formation: The first step in the formulation of tablet in capsule approach was to select the appropriate capsule size that can accommodate optimized batches of enteric coated tablet and immediate release blend for the purpose, capsule 0.00 was selected according to specifications given by USP. Size 0.00 capsule can accommodate enteric coated ibuprofen tablet weighing 200 mg and immediate release omeprazole pills 20 mg.

RESULTS AND DISCUSSION:

4.1 Preformulation/Precompression Parameters:

- ✓ **Bulk Density:** Bulk density of the powder blend F1, F2, F3, F4, range from 0.5760gm/cm3, 0.6920gm/cm3, 0.5625gm/cm3 respectively. Each value represents mean value of three determinations. (Table-1)

- ✓ **Carr's Index:** Carr's index for the powder blend F1, F2, F3, F4 range from 13.4%, 15%, 20%, 25%, respectively. Each value represents mean value of three determinations. (Table-1)

- ✓ **Angle Of Repose:** The '0' value which represents the angle of repose for the powder blend F1, F2, F3, F4, were found be 25.30, 30.02, 32.40, 26.15 respectively. Each value represents mean value of three determinations. (Table-1)

- ✓ **Hausner Ratio:** Hausner ratio for the blend F1, F2, F3, F4 were found to be 1.144, 1.1764, 1.25,

and 1.333, respectively. Each value represents mean value of three determinations.

- ✓ **Drug - Excipients Compatibility Studies:** The pure drug ibuprofen and the omeprazole is used in the preparation of formulations were characterized by FTIR spectroscopy to know the compatibility as shown in figure no 11-20. There was no significant difference in the FTIR spectra of pure drug ibuprofen and the formulations.

Table No: 1 Preformulation Parameter

Formulation	Bulk Density (Gm/Cm)	Carr's Index (%)	Angle of Repose	Hausner's Ratio
F1	0.5760	13.4	25.30	1.1779
F2	0.6920	15	30.02	1.1764
F3	0.5625	20	32.40	1.25
F4	0.7410	25	26.15	1.333

4.2 Method of Formulation of Ibuprofen Conventional Tablets:

Four batches F1, F2, F3, F4 of combined capsule were formulated atdifferent drug and polymer ratio (5%, 20% HPMC, lactose and magnesium serrate) as base along with other polymer (1:1, 1:2, 1:3, 1:4) respectively.

4.2 Evaluation Of Combined Capsule:

- ✓ **Drug Content Uniformity: Standard graph:** Standard graph for the drug ibuprofen and omeprazole was plotted using 0.01N Hcl. The linearity was best observed in the concentration range of 1-20µg/ml. Y=0.008x; R2=0.991 Drug **content uniformity:** Drug content of the formulated combined capsule of ibuprofen and omeprazole pills F1, F2, F3, F4 were found to be 96mg, 94mg, 95mg, 93mg respectively. Each value represents mean value of three determinations.

- ✓ **Hardness:** Hardness of the formulated (F1, F2, F3, F4) combined capsule of ibuprofen and omeprazole pills found to be 1.3kg/cm², 2.5 kg/cm², 6 kg/cm², 5.5 kg/cm².

- ✓ **Friability:** Friability of the formulated combined capsule was found byroche friabilator. The percentage weight loss range from 0.1%, 0.2%, 0.3%, 0.4% for batches F1, F2, F3, F4 respectively. Each value represents mean value of three determinations.

- ✓ **Disintegration analysis:** Disintegration of the formulated F1, F2, F3, and F4 combined capsule of ibuprofen and omeprazole pills found to be 115sec, 168sec, 225sec, and 295sec respectively. Each value represents mean value of four determinations.

- ✓ **Weight variation analysis:** The percentage weight variation for the formulated combined capsule were found to be in the range of ±7.5%.

- ✓ **In vitro drug release study:** The percentage drug release at the end of the 30 min for the formulated in combined capsule F1, F2, F3, F4 were found to be respectively each value represent mean 90%, 84%, 80%, 75% value of four determination's

Table No: 2 Concentration & The Absorbance for The Drug Ibuprofen (Standard Graph)

Concentrtion (mcg)	Absorbance
2	0.014
4	0.016
6	0.028
8	0.032
10	0.038

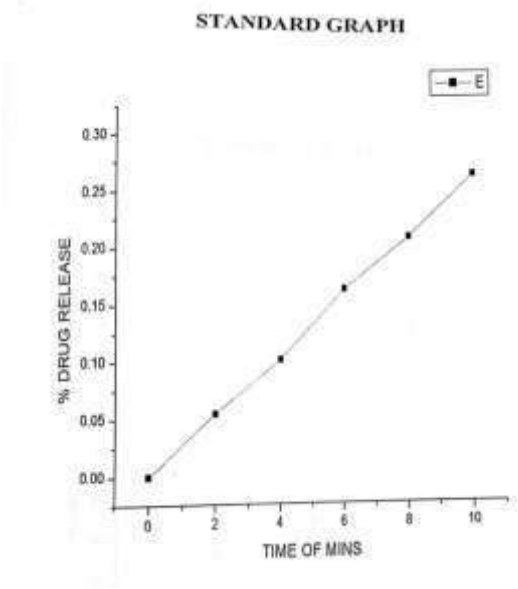

Fig: 3 Standard Graph

Table No: 3 Procedure For Determination Of Drug Content Uniformity

Formulation	Procedure
F1	Amount equivalent to 100mg of drug 0.1531gms of (average weight) powdered tablet was transferred in 100ml standard flask and followed as in procedure for drug content determination.
F2	Amount equivalent to 100mg of drug 0.1493gms of (average weight) powdered tablet was transferred in 100ml standard flask and followed as in procedure for drug content determination.
F3	Amount equivalent to 100mg of drug 0.1522gms of (average weight) powdered tablet was transferred in 100ml standard flask and followed as in procedure for drug content determination.
F4	Amount equivalent to 100mg of drug 0.1495gms of (average weight) powdered tablet was transferred in 100ml standard flask and followed as in procedure for drug content determination.

Table No: 4 Capsule Content Uniformity

Formulation	Content (mg)	Percentage Of Content
F1	96	96%
F2	94	94%
F3	95	95%
F4	93	93%

Table No: 5 Evaluation

Formulation	Hardness (kg/cm^2)	Friability	Disintigration Time (sec)
F1	1.3(kg/cm^2)	0.1(+-)0.009	115
F2	2.5(kg/cm^2)	0.2(+-)0.007	168
F3	6(kg/cm^2)	0.3(+-)0.012	228
F4	5.5(kg/cm^2)	0.4(+-)0.017	295

Table No: 6 Weight Variation Analysis

Sr. No	F1 (gms)	F2(gms)	F3(gms)	F4(gms)
1	0.1514	0.1424	0.1518	0.1434
2	0.1510	0.1421	0.1512	0.1443
3	0.1507	0.1418	0.1532	0.1456
4	0.1523	0.1458	0.1542	0.1476
5	0.1521	0.1456	0.1533	0.1454
6	0.1524	0.1454	0.1539	0.1432
7	0.1514	0.1444	0.1527	0.1416
8	0.1516	0.1463	0.1534	0.1434
9	0.1517	0.1432	0.1516	0.1427
10	0.1523	0.1414	0.1523	0.1438
11	0.1526	0.1432	0.1554	0.1432
12	0.1516	0.1424	0.1534	0.1431
13	0.1518	0.1412	0.1526	0.1438
14	0.1519	0.1465	0.1543	0.1432
15	0.1522	0.1445	0.1565	0.1438
16	0.1529	0.1423	0.1554	0.1413
17	0.1519	0.1454	0.1514	0.1421
18	0.1521	0.1443	0.1532	0.1427
19	0.1520	0.1456	0.1554	0.1453
20	0.1522	0.1421	0.1534	0.1415
Average Weight F1 – F4 (gms)				
21	0.1523	0.1431	0.1542	0.1441

Table No: 7 In Vitro Drug Release (F1-Formulation)

F1 Formulation		
Time in Mins	**Amount of Drug (mg)**	**% Of Drug Release**
5	52	52%
10	58	58%
15	64	64%
20	78	78%
25	84	84%
30	90	90%

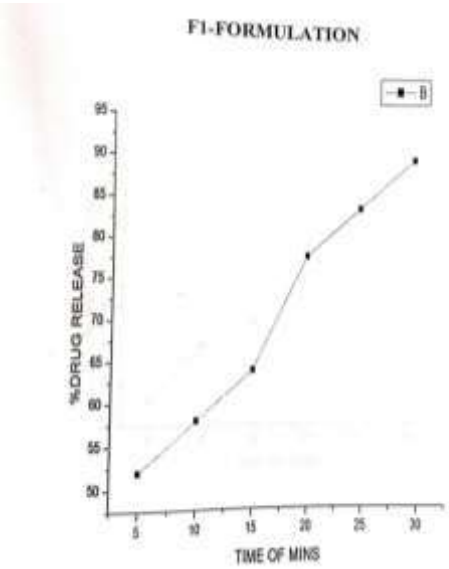

Fig: 4 In Vitro Drug Release (F1-Formulation)

Table No: 8 In Vitro Drug Release (F2-Formulation)

F2 Formulation		
Time In Mins	**Amount of Drug**	**% Of Drug Release**
5	48	48%
10	55	55%
15	58	58%
20	64	64%
25	76	76%
30	84	84%

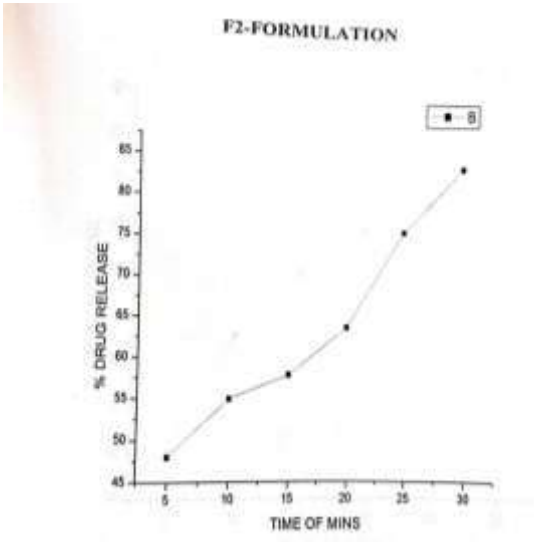

Fig: 5 In Vitro Drug Release (F2-Formulation)

Table No: 9 In Vitro Drug Release (F3-Formulation)

F3 Formulation		
Time In Mins	**Amount Of Drug**	**% Of Drug Release**
5	45	45%
10	50	50%
15	56	56%
20	60	60%
25	68	68%
30	80	80%

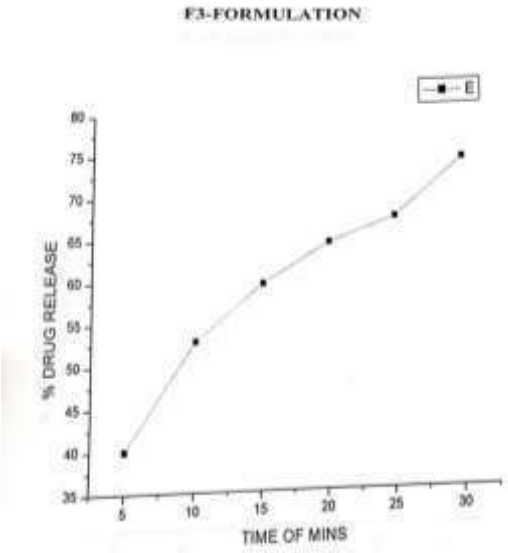

Fig: 6 In Vitro Drug Release (F3-Formulation)

Table No: 10 In Vitro Drug Release (F4-Formulation)

F4 Formulation		
Time In Mins	**Amount Of Drug**	**% Of Drug Release**
5	40	40%
10	53	53%
15	60	60%
20	65	65%
25	68	68%
30	75	75%

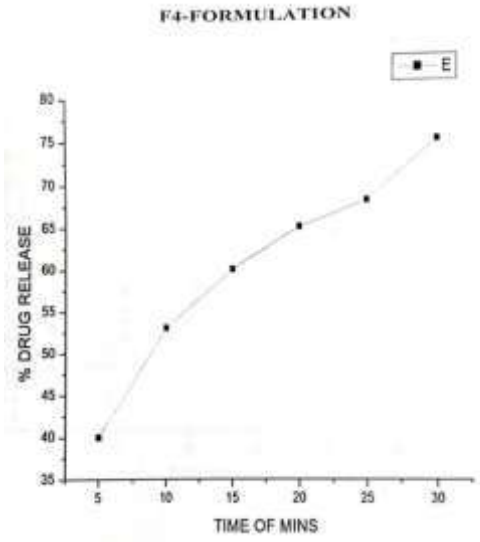

Fig: 7 In Vitro Drug Release (F4-Formulation)

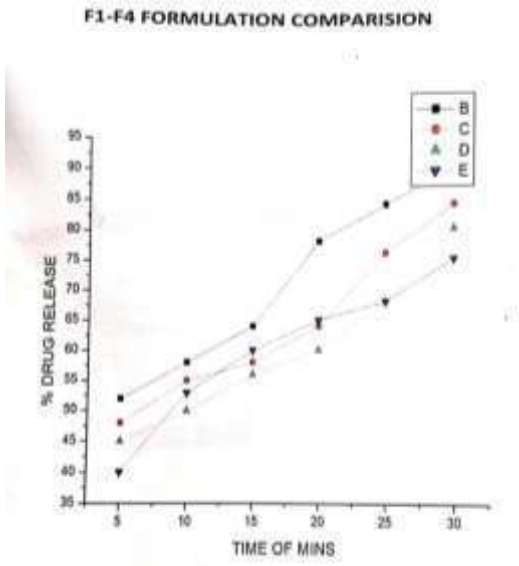

Fig: 8 In Vitro Drug Release (F1-F4)

CONCLUSION:

Combined capsule of ibuprofen and omeprazole pills prepared by compression method and subject to disintegration studies & in vitro drug release studies. The characterised for two drugs were study was also pre-formulation studies was also carried out the disintegration time for four formulations were observed. F1 shows the better disintegration than F2, F3 and F4. The disintegration time for F1 is found to be 2mins. In-vitro dissolution profile also showed that F1 has the better percentage drug release when compared to the F2. The formulation F1 combined capsule of ibuprofen and omeprazole pills release was

found to be 90% The combined capsule of ibuprofen and omeprazole pillsF2, F3, F4 shows the lower disintegration time and % of drug release than F1.

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