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Formulation and Evaluation of Effervescent Tablets Paracetamol

Meenali Mishra*[1], Dr.(Prof) Kaushal K.Chandrul [2], Sarita Sharma[3],Dr.Hariom Sharma[4], Dr.Gaurav Kumar Sharma[5]

1. M.Pharma Research Scholar,Mewar University,Gangrar,Rajasthan,India.
2. Professor and Principal,Dept.Of Pharmacy,Mewar University,Gangrar,India.
3. Assistant Professor,Dept Of Pharmacy,Mewar University,Gangrar,India.
4. Professor,Dept Of Pharmacy,Mewar University,Gangrar,India.
5. Associate Professor,Dept Of Pharmacy,Mewar University,Gangrar,India.

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ABSTRACT
Espite some drawbacks including sluggish absorption,which prolongs the beginning of effect, oral dosage forms remain the most common method of pharmaceutical administration.The medicine can be administered in liquid form to get around this, however many APIs only have a limited amount of stability in liquid form. Effervescent Tablets serve as a substitute dose form as a result.The combination of tartaric acid and citric acid with alkali metal carbonates or bicarbonates in the presence of water causes the tablet to swiftly break apart by internal CO2 liberation in water.The breakdown of API in water as well as the taste-masking effect are improved as a result of CO2 gas liberation. In the current work, an effort has been made to use a variety of acids and bases to create an effervescent tablet that releases paracetamol immediately.Wet granulation was used in the formulation of tablets together with dry granulation since it was deemed to be an appropriate method.The preparation and evaluation of the nine placebo tablets' hardness, time to disintegrate, weight fluctuation, and solubility.The mixture of citric acid (12.55 percent),tartaric acid (24.16 percent),sodium bicarbonate (38.25 percent),sodium carbonate (7.41 percent),binding agent PVP-K-30 (3.94 percent),sodium benzoate, however, exhibits the greatest hardness and weight fluctuation within the acceptable range (0.55 percent).In the formulation's final form (F7) Due to the good effervescent reaction and lack of issues with capping and adhering compared to other formulations, these substances.

Key words: oral mucosa, mucin, and bioadhesio

I. INTRODUCTION

Effervescent tablets

Carbon tablets, often known as effervescent tablets, are tablets that dissolve in water and release carbon dioxide. They are the result of compressing powdered component components into a dense mass, which is then packaged in a blister pack or a hermetically sealed packaging with a desiccant in the cap.To use them, simply submerge them in water to create a solution.The powdered materials can either be granulated and sold as effervescent granules or packed as effervescent powders. Before being turned into tablets, powdered components are usually granulized first. Effervescent medical beverages first appeared in the late 1800s to hide the taste of bitter waters used as cures during the fad for water cures at the time.

For decades, effervescence has been used in the pharmaceutical and dietary sectors as an oral medication delivery mechanism. Effervescent dosage forms are common in Europe, and their popularity is expanding in the United States because they allow pharmaceutical and nutraceutical companies to expand their market share. Over the years, a variety of effervescent pills have been developed. Dental enzyme compositions, contact lens cleaners, washing powder compositions, beverage sweetening tablets, chewable dentifrice, dental cleansers, surgical instrument sterilisers, analgesics and effervescent candies, as well as many preparations of prescription pharmaceuticals such as antibiotics, ergotamines, digoxin, methadone, and L-dopa, are among them. Veterinary preparations have also been produced.

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There are a number of active substances that are best delivered in the form of effervescent formulations, including:

1.Those that are difficult to digest or cause stomach or esophageal irritation

2.Amino acids and antibiotics, for example, are pH sensitive.

3.Those who require a high dose.

4.Those that are light,oxygen, or moisture sensitive.

5.It's a gastrointestinal stimulant.

By elevating gastric pH and so hastening the emptying of medication into the small intestine, effervescent formulations may improve absorption and speed up commencement of action.By opening up paracellular transport, the carbon dioxide bubbles may also aid intestine absorption.When comparing effervescent tablets to conventional tablets,extreme bioavailability discrepancies of up to 4 fold have been recorded, underscoring the need for additional bioequivalence studies when switching dosage forms. It's risky to swallow an effervescent tablet whole since it can become caught in the subglottis and fizzle there. Irritation can lead to a possibly deadly edoema. Furthermore, ordinary effervescent pills contain a substantial quantity of sodium and, according to a 2013 study, are linked to an elevated risk of severe cardiovascular events. There are sodium-free or low-sodium formulas available.

Reason for selection effervescent tablets of paracetamol

1.Fast onset of action: The medication substance is already in solution when the effervescent tablet is taken, which is a significant advantage. As a result, absorption is faster and more thorough than with a traditional tablet. This is especially useful for managing acute pain problems. Faster absorption means faster action, which is important when treating acute symptoms like pain. Formula performance is enhanced by buffered preparations with changeable stomach pH. Effervescent medications are supplied to the stomach at just the optimum pH for absorption. Many medications take a long time to pass through the gastrointestinal tract or are impeded in their absorption by food or other medications. Such medications must be given as injections or in higher doses in order to attain desired absorption levels.

2.No need to swallow tablets:Effervescent drugs are given in liquid form, making them easier to absorb than pills or capsules.The number of people who can't or don't like taking tablets and capsules is on the rise.Many diseases necessitate the patient or client swallowing multiple medications at once.Tablets are particularly difficult to swallow for the elderly. One dose of an effervescent dosage form can usually be administered in as little as 3 or 4 ounces of water. When someone swallows a traditional tablet or capsule, this is the amount used.

3.Good stomach and intestinal tolerance: In a buffered solution, effervescent pills completely dissolve. Reduced localised contact in the upper GI tract causes reduced discomfort and improves tolerability. Buffering also prevents gastric acids from reacting with the medications, which can cause serious stomach and esophageal problems.

4.More portability: Because no water is added until the drug is ready to use, effervescent pills are easier to transport than liquid medication.

5.Improved palatability: Most liquids, mixes, and suspensions taste better than drugs administered with the effervescent base. By reducing undesirable qualities and complimenting compositions with tastes and scents, superior taste masking can be accomplished. After a long period of storage, effervescent medications keep their flavour. The flavourings in the effervescent tablets make them taste considerably better than a non-effervescent powder mixed with water. Furthermore, they manufacture effervescent pills, which may appeal to consumers more than standard dose forms.

6.Superior stability: Effervescent compositions have exceptional stability, far beyond that of liquid forms.

7.More consistent response: The pharmacokinetic characteristics of drugs administered by effervescent technology are far more predictable and reproducible than those of tablets or capsules.

8.Incorporation of large amounts of active ingredients: In many circumstances, one effervescent tablet will provide the same active dose as three conventional tablets.

9.Accurate dosing: When compared to traditional formulations, effervescent tablets improve the absorption of a variety of active substances (such

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as disulfiram and caffeine). This is because the carbon dioxide produced by the effervescent reaction can modify the paracellular route, resulting in increased active-ingredient permeability. The principal route of absorption for hydrophilic active components is the paracellular pathway, in which the solutes diffuse into the intercellular space between epithelial cells.Carbon dioxide is thought to enlarge the intercellular space between cells, allowing for higher absorption of active substances (both hydrophobic and hydrophilic).The higher absorption of hydrophobic active substances could be due to non-polar carbon dioxide gas molecules partitioning into the cell membrane, resulting in a more hydrophobic environment, allowing the hydrophobic active ingredients to be absorbed more effectively.

10. Improved therapeutic effect: The active compounds' therapeutic properties are improved because to the effervescent components. They also aid in the solubilization of medications that are difficult to dissolve.

Materials and methods: List of materials

S. No	**Ingredients**	**Company**
1	Paracetamol	API
2	Citric acid	Qualigens fine chemical
3	Sodium citrate	Qualigens fine chemical
4	Acesulfum potassium	Spectrum chemical
5	Tartaric acid	Spectrum chemical
6	Sodium bicarbonate (anhydrous)	Rankem
7	Sodium carbonate	Spectrum chemical
8	Ascorbic acid	ACS chemical
9	Polyethylene Glycol-6000	FUJIFILM Wako Pure Chemical Corporation
10	Polyvinylpyrollidone-30	Ottokemi
11	Fumaric acid	Spectrum
12	Sodium Benzoate	ULTRA PURE LAB CHEM
13	Sodium lauryl sulphate	CDH
14	Mannitol	Rankem

PRE-FORMULATION STUDIES

Pre-formulation is a discipline of pharmaceutical research that involves determining the physicochemical properties of a drug material using biopharmaceutical principles. Pre-formulation studies are used to determine the best form of a chemical, analyse its physical qualities, and gain a thorough understanding of the material's stability under diverse situations, resulting in the best medication delivery system. The preformulation research focuses on the physiochemical variables that may influence the production of an effective dosage form. These characteristics may eventually provide a reason for formulation development. It will also aid in minimising issues in later phases of drug development, lowering drug development expenses, and shortening the time it takes for a product to reach market. It provides the necessary information to characterise the nature of the drug substance and

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establish a framework for its use.In the dose form, the medication is combined with pharmaceutical excipients.

The use of preformulation parameters increases the likelihood of formulating a product that is acceptable, safe, efficacious, and stable.

At the very least, the tests listed below are included in preformulation.

i. Bulk Characterization

powder qualities (flow, compaction, density, particle size, surface area, etc.) crystallinity, polymorphism, and hygroscopicity microscopic examination (morphology, particle characteristics) spectroscopy of molecules (ft-ir)

ii. Solubility Analysis Solubility is a term used to describe the ability of a substance to dissolve in water.

ph heat effect on solubility solubility profile common ion effect

dissolution of solubilization

iii. Stability Analysis solution stability (heat, light, acid, base, oxidizer)solid-state stability ,excipient compatibility

Consideration in the formulation of effervescent tablets:

There are various elements that influence the drug release from effervescent tablets.

a) dosage
b) Solubility
c) particle size

Drug-excipient compatibility study: The following excipients used in the studies were evaluated for drug-excipient compatibility

S no	Excipient	category
1	Citric acid	acidifying agent
2	Sodium citrate	buffering agent
3	Tartaric acid	acidifying agent
4	Sodium bicarbonate (anhydrous)	alkalizing agent
5	Sodium carbonate	alkalizing agent
6	Ascorbic acid	antioxidant
7	Polyethylene Glycol-6000	binding agent.
8	Polyvinylpyrollidone-30	binding agent.
9	Fumaric acid	acidulant
10	Sodium Benzoate	lubricant
11	Sodium lauryl sulphate	lubricant
12	Mannitol	binding agent
13	Acesulfum potassium	sweetener

These excipients were combined in varying ratios depending on the functional category. These mixes were held at 40°C 76 percent RH and 45°C 76 percent RH, respectively.

The sample was withdrawn after a four-week period and subjected to analysis and associated compounds. The samples were taken at two-week and four-week intervals and analysed for the following parameters:

1. Moisture content
2. Assay
3. Related substances

Based on the findings, the following excipients were finally chosen to create a stable prototype formulation of paracetamol effervescent tablets

Selected Excipients for Prototype Formulation:

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TABLE NO-2

S.NO.	Excipients
1	Citric acid
2	Tartaric acid
3	Fumaric acid
4	Acesulfum potassium
5	Sodium benzoate
6	Sodium lauryl sulphate
7	Sodium citrate
8	Mannitol
9	Polyethylene glycol-6000
10	Polyvinylpyrollidone-30
11	Sodium carbonate
12	Sodium bicarbonate
13	Ascorbic acid

A. Evaluation of Granules of PARACETAMOL

1) Angle of repose
2) Bulk density
3) Tapped density
4) Compressibility

I) EVALUATION OF GRANULES

Compactness, physical stability, rapid production capability, chemical stability, and efficacy are the perfect properties of a tablet that make it a popular and accepted dosage form. In general, the quality of the granulation from which the tablet is formed determines the above properties.

There are numerous formulation and process variables to consider.The features of the granulation produced can be influenced by the granulation stage. To assess granulation appropriateness for tableting, numerous methods to measure specific granulation parameters have been devised. Flow properties and compressibility are the most important granulation features to keep an eye on.

Angle of repose: The angle of repose was determined using the fixed funnel method. The fixed funnel method calls for securing a funnel with its tip at a specific height H above graph paper on a flat horizontal surface. The granules were gently poured down the funnel until the conical pile's peak just touched the funnel's tip. As a result, where R is the radius of the conical pile's base.

Tan α = H/R Where, α = Angle Of Repose

Apparent Bulk Density: (δu)

With the use of a funnel, a correctly weighed sample of granulation was carefully added to the measurement cylinder. The volume was then noted. In an instrument consisting of a graduated cylinder fixed on a mechanical tapping device, the volume of the packing was determined. The following formula is used to calculate apparent bulk density:-

δU = M /VU

Where, M = Mass Of Granulation In Gms

Vu = volume of granulation (initial untapped volume)

Packed Bulk Density: (δb)

The procedure outlined above was followed. The ultimate volume was tapped until there was no more drop in volume.

The following formula is used to calculate packed bulk density.

b = m/vb

where, m = mass of granulation in gms

Vb = volume of granulation (final tapped volume)

PERCENT COMPRESSIBILITY: (%C)

It's a crucial metric that can be calculated from bulk density readings. The % compressibility was calculated using the formula below.

c = δb - δu/δb x 100

where, δb = packed bulk density

δu = apparent bulk density

Evaluation of effervescent compressed tablets

i. tablet shape & dimensions
ii. hardness
iii. thickness

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iv. friability
v. weight variations
vi. disintegration time
vii. content uniformity of active
viii. ingredients
ix. in-vitro drug release
x. comparison with marketed
xi. conventional tablet

TABLET DIMENSIONS:

A calibrated dial calliper was used to measure the thickness and diameter of the table. Each formulation was tested with ten tablets.

HARDNESS:

A Monsanto hardness tester was used to assess the tablet's hardness. The tester is made out of a barrel with a compressible spring sandwiched between two plungers.

zero reading was taken by placing the bottom plunger in contact with the tablet.

By rotating a threaded bold, the upper plunger was pressed against a spring until the tablet fractured. A pointer rides along a gauge in the barrel as the spring compresses, indicating the force. The fracture force was measured, and the zero force reading was subtracted. Each formulation's ten pills were tested.

FRIABILITY:

Roche friabilator :

The friability of the tablets was determined using the Roche friabilator. The friabilator was filled with twenty preweighed tablets and turned for 100 revolutions. After that, the tablets were dusted and reweighed. The friability was calculated using the formula:

$F = 100 (1 – Wo) /W$

where, f = percentage friability

wo = initial weight of 20 tablets

w = weight after friability testing

WEIGHT VARIATION:

A total of twenty tablets were chosen at random. The average weight of the tablets was estimated after they were individually weighed. After that, the % departure of each tablet from the average weight was calculated.

Preformulation study:

To guarantee that the drug was compatible with the excipients, IR spectra for the pure drug and produced granules were collected and compared to ensure that the principle peaks did not change - preventing interference and possible degradation.

The peaks found in produced formulation granules were nearly identical to those obtained in pure drug, indicating that there was no interaction between drug and acids, bases, or other substances.

PROTYPE FORMULATIONS BY DIRECT COMPRESSION: -

FORMULA-1

TABLE NO-3

S.no	Ingredients	Qty.(mg)	%w/w
1	paracetamol	500	35.36
2	citric acid (anhydrus)	232.63	16.91
3	ascorbic acid	201	14.75
4	sodium bicarbonate	278.86	19.10
5	sodium citrate	201	14.75
6	peg-6000	35	2.05
7	polyvinylpyrolidone-k-30	15	1.033

All Quantity in mg/tablet. COMPRESSION WEIGHT OF TABLET 1463.2MG/TAB

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FORMULA- 2

TABLE NO-4

S.NO	Ingredients	Qty.(mg)	%w/w
1	paracetamol	500	35.55
2	Citric acid(anhydrus)	105.5	7.522
3	Tartaric acid	202	15.22
4	Sodium bicarbonate	332.5	25.05
5	Polyvinyl pyrolidone-k30	20	1.25
6	Sodium lauryl sulphate	19	1.25
7	aerosil	07	0.427
8	mannitol	209	1.478

All Quantity in mg/tablet. COMPRESSION WEIGHT OF TABLET - 1395MG/TAB

FORMULA- 3

TABLE NO-5

S.no	Ingredints	Qty.(mg)	%w/w
1	Paracetamol	500	35.85
2	citric acid(anhydrus)	105.6	6.25
3	tartaric acid	205	15.01
4	sodium bicarbonate	355.5	25.55
5	sodium carbonate	19	13.56
6	sodium citrate	22	1.495
7	mannitol	209	15.50
8	polyvinylpyrolidone-k-30	21	1.395
9	acesulphum potassium	11	0.698

All Quantity in mg/tablet. COMPRESSION WEIGHT OF TABLET – 1448.1 MG/TAB

FORMULA – 4

TABLE NO-6

S.no	Ingredients	Qty.(mg)	%w/w
1	Paracetamol	500	11.85
2	citric acid(anhydrus)	525	12.35
3	tartaric acid	1046	25.75
4	sodium bicarbonate	1575	38.25
5	sodium carbonate	266	6.273
6	sodium citrate	19	0.43

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7	mannitol	209	5.92
8	polyvinylpyrolidone-k-30	70	1.43
9	acesulphum potassium	21	0.48

All Quantity in mg/tablet. COMPRESSION WEIGHT OF TABLET – 4231 MG/TAB

FORMULA – 5

TABLE NO-7

S.no	Ingredients	Qty(mg)	%w/w
1	paracetamol	500	13.45
2	citric acid (anhydrus)	488	13.11
3	tartaric acid	983	25.52
4	sodium bicarbonate	1485	38.03
5	sodium carbonate	255	5.24
6	sodium benzoate	12	0.25
7	mannitol	250	6.45
8	polyethylene glycol-6000	45	0.99
9	acesulphum potassium	20	0.50

All Quantity in mg/tablet. COMPRESSION WEIGHT OF TABLET - 4038 MG/TAB

FORMULA- 6

TABLE NO-8

S.no	Ingredients	Qty(mg)	%w/w
1	Paracetamol	500	13.2
2	citric acid(anhydrus)	488	12.11
3	tartaric acid	985	25.55
4	sodium bicarbonate	1489	38.08
5	sodium carbonate	255	7.25
6	sodium citrate	20	0.39
7	mannitol	230	6.62
8	polyvinylpyrolidone-k-30	70	1.6

All Quantity in mg/tablet. COMPRESSION WEIGHT OF TABLET - 4037 MG/TAB

FORMULA-7

TABLE NO-9

S.no	Ingredients	Qty(mg)	%w/w
1	Paracetamol	500	12.75
2	citric acid(anhydrus)	495	12.51
3	tartaric acid	985	25.89
4	sodium bicarbonate	1585	39.83
5	sodium carbonate	265	6.39

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6	sodium citrate	25	0.55
7	polyvinylpyrolidone-k-30	120	2.95
8	acesulphum potassium	35	0.85

All Quantity in mg/tablet.
COMPRESSION WEIGHT OF TABLET – 4010 MG/TAB

FORMULA - 8

TABLE NO-10

S.no	Ingredients	Qty(mg)	%w/w
1	Paracetamol	500	13.45
2	citric acid(anhydrus)	495	12.85
3	tartaric acid	985	30.95
4	sodium bicarbonate	1500	38.45
5	sodium carbonate	250	6.45
6	sodium citrate	30	0.65
7	polyvinylpyrolidone-k-30	35	2.35
8	acesulphum potassium	25	0.55

All Quantity in mg/tablet.
COMPRESSION WEIGHT OF TABLET - 3820 MG/TAB

FORMULA-9

TABLE NO-11

S.no	Ingredients	Qty(mg)	%w/w
1	Paracetamol	500	13.55
2	citric acid(anhydrus)	485	12.95
3	tartaric acid	965	25.99
4	sodium bicarbonate	1355	38.55
5	sodium carbonate	215	5.70
6	sodium citrate	35	0.85
7	polyvinylpyrolidone-k-30	105	2.75
8	acesulphum potassium	20	0.45

All Quantity in mg/tablet
COMPRESSION WEIGHT OF TABLET - 3680 MG/TAB

Wet Granulation:
The process of wet granulation is divided into three stages.

a. Dry Mixing & Granulation
b. Lubrication of Granules
c. Compression of Lubricated Granules

Dry mixing and granulation: The dry mixing and granulation method has two steps: acid granulation and base granulation.

1) Acid granulation

(l) In the first phase, the Citric and Tartaric acids were mixed and passed through Sieve No. 40 by weight.

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(ii) The second stage involved dissolving simethicone in an organic solvent, such as methylene chloride.
The organic solvent was combined with acid components, such as citric acid and tartaric acid. The acquired wet mass was sieved no. 20 and dried in a tray at 600 degrees Celsius for 1 hour, until the L.O.D. was less than 1%. (For 5 minutes on IR at 1050 C)

Base granulation:
(i) First, the sodium bicarbonate and sodium carbonate were combined and passed through sieve no. 40 in the base granulation.
(ii) The binding agent PVP-K-30 was dissolved in an organic solvent, methylene chloride, in the second step.
The aforesaid organic solvent was combined with sodium bicarbonate and sodium carbonate as base components. The acquired wet mass was sieved no. 20 and dried in a tray at 600 degrees Celsius for 1 hour, until the L.O.D. was less than 1%. (For 5 minutes on IR at 1050 C)
Lubrication of acid and base granules: - both granules, acid and basic granules, were combined after drying at R.T. After thoroughly combining both granules, add the paracetamol, potassium acesulfate, and lubricant sodium benzoate to the granules.
Compression of Lubricated Granules: Using a single rotary tablet, the lubricated granules were compressed into tablets.Punching machine, 12 stations, with 24.8mm punch sets.

PROTYPE FORMULATIONS BY WET GRANULATION: -
FORMULA-1

TABLE NO-12

S.no	Ingredients	Qty(mg)	%w/w
1	Paracetamol	500	35.38
2	citric acid(anhydrus)	235.65	16.92
3	ascorbic acid	250	14.75
4	sodium bicarbonate	279.89	19.15
5	sodium citrate	250	14.75
6	Peg-6000	35	2.08
7	polyvinylpyrolidone-k-30	20	1.032

All Quantity in mg/tablet
COMPRESSION WEIGHT OF TABLET – 1570.5MG/TAB

FORMULA-2

TABLE NO-13

S.no	Ingredients	Qty(mg)	%w/w
1	Paracetamol	500	35.52
2	citric acid(anhydrus)	105.5	7.422
3	tartaric acid	205	15.25
4	sodium bicarbonate	355.5	26.05
5	polyvinylpyrolidone-k-30	20	1.29
6	sodium lauryl sulphate	15	1.29
7	aerosil	10	4.28
8	mannitol	209	1.475

All Quantity in mg/tablet. COMPRESSION WEIGHT OF TABLET - 1231.9 MG/TAB

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FORMULA-3

TABLE NO-14

S.no	Ingredients	Qty(mg)	%w/w
1	Paracetamol	500	12.82
2	citric acid(anhydrus)	525	13.30
3	tartaric acid	1049	24.75
4	sodium bicarbonate	1577	37.30
5	sodium carbonate	269	6.275
6	sodium benzoate	20	0.45
7	mannitol	210	4.95
8	polyvinylpyrolidone-k-30	70	1.45
9	simethicone	20	0.38
10	acesulphum potassium	25	0.49

All Quantity in mg/tablet. COMPRESSION WEIGHT OF TABLET – 4265 MG/TAB

FORMULA-5

TABLE NO-16

S.no	Ingredients	Qty(mg)	%w/w
1	Paracetamol	500	12.50
2	citric acid(anhydrus)	490	12.15
3	tartaric acid	990	25.52
4	sodium bicarbonate	1583	38.03
5	sodium carbonate	255	7.25
6	sodium benzoate	15	0.25
7	mannitol	225	6.49
8	Polyethylene giycol-6000	45	0.98
9	simethicone	20	0.38
10	acesulphum potassium	25	0.49

All Quantity in mg/tablet. COMPRESSION WEIGHT OF TABLET - 4148 MG/TAB

FORMULA- 6

TABLE NO-17

S.no	Ingredients	Qty(mg)	%w/w
1	Paracetamol	500	12.8
2	citric acid(anhydrus)	488	12.11
3	tartaric acid	985	24.56
4	sodium bicarbonate	1485	38.08
5	sodium carbonate	255	7.28
6	sodium benzoate	20	0.39
7	mannitol	230	6.62
8	polyvinylpyrolidone-k-30	70	1.9

All Quantity in mg/tablet. COMPRESSION WEIGHT OF TABLET - 4033MG/TAB

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FORMULA-7

TABLE-18

S.no	Ingredients	Qty(mg)	%w/w
1	Paracetamol	500	12.75
2	citric acid(anhydrus)	495	12.49
3	tartaric acid	985	25.99
4	sodium bicarbonate	1489	38.33
5	sodium carbonate	255	7.36
6	sodium benzoate	25	0.51
7	Simethicone	65	2.95
8	Polyvinylpyrolidone-k-30	120	1.55
9	Acesulphum potassium	35	0.77

All Quantity in mg/tablet. COMPRESSION WEIGHT OF TABLET – 3969MG/TAB

FORMULA – 8

TABLE NO-19

S.no	Ingredients	Qty(mg)	%w/w
1	Paracetamol	500	13.38
2	citric acid(anhydrus)	485	12.85
3	tartaric acid	975	30.95
4	sodium bicarbonate	1500	38.45
5	sodium carbonate	245	6.45
6	sodium benzoate	30	0.65
7	Simethicone	35	2.32
8	Polyvinylpyrolidone-k-30	30	0.67
9	Acesulphum potassium	25	0.55

All Quantity in mg/tablet. COMPRESSION WEIGHT OF TABLET - 3825 MG/TAB

FORMULA - 9

TABLE NO-20

S.no	Ingredients	Qty(mg)	%w/w
1	Paracetamol	500	13.55
2	citric acid(anhydrus)	495	13.99
3	tartaric acid	975	25.99
4	sodium bicarbonate	1425	38.55
5	sodium carbonate	225	6.39
6	sodium benzoate	45	0.91
7	Simethicone	65	1.45

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8	Polyvinylpyrolidone-k-30	105	2.85
9	Acesulphum potassium	25	0.45

All Quantity in mg/tablet. COMPRESSION WEIGHT OF TABLET -3860 MG/TAB

TABLE NO – 21

Formula A	**Observation**	
	DIRECT COMPRESSION	**WET GRANULATION**
F1	Capping problem,less effervescence	Capping problem,less effervescenc
F2	Capping problem,less effervescence	Capping problem,less effervescence
F3	Capping problem,less effervescence	Capping problem,less effervescence
F4	The effervescence of the tablets is quite fast, however the tablet surface is rough.	In comparison to direct compression, tablets with rapid effervescence have a smoother surface.
F5	The tablet produces good effervescence, however some particles land at the bottom of the solution, causing a capping difficulty.	Tablet produces a good amount of effervescence, the solution becomes somewhat clearer, and there is less of a capping problem.
F6	Tablets provide good effervescence, but they also have a capping issue.	The capping also contributes to the effervescence of the tablet.
F7	The tablet has a nice effervescence, no capping issues, but some particles settle down, and the hardness is poor.	The tablet has good effervescence, no capping issues, and the solution is clear. The tablet's hardness is also good when compared to other batches.
F8	The tablet was determined to have a good hardness, but there was some capping issues, and the remedy was not evident.	The tablet has good effervescence, no capping issues, and the solution is clear. However, the tablet's hardness is poor.
F9	The tablet produces a gentle effervescent effect. Other qualities, like as hardness and aesthetics, are less desirable.	The tablet produces a gentle effervescent effect.Other characteristics, like as hardness and look, are satisfactory.

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Simethicone was not employed in direct compression. However, it was used in the wet granulation process.

According to the results of the investigation, wet granulation provides good tablet properties and was chosen as the final formulation for the manufacturing of Effervescent tablets

II. RESULTS

A preformulation study was conducted on the medication and excipients prior to formulation. The formulation process is broken down into four steps in. First, placebo tablets were created with various acids and bases in various quantities. In the table, the detailed composition is shown. Angle of repose, bulk density, and tapped density were all measured on the granules. Physical properties of the placebo pills were assessed, including thickness, hardness, friability, weight fluctuation, disintegration, and solubility. The best acid base combination, as well as a variety of other water-soluble substances, were chosen.

The tablets were then made in the second phase using a variety of acid base concentrations. Table no. 1 shows the detailed composition. Angle of repose, bulk density, and tapped density were all measured on the granules. The tablets were tested for thickness, hardness, friability, weight fluctuation, and disintegration, among other physical characteristics. The findings were found to be equivalent to those seen in pre-formulation experiments. Citric acid 12.5 percent, tartaric acid 25.17 percent, sodium bicarbonate 38.02 percent, and sodium carbonate 6.41 percent were the final proportions of the major excipients determined by this investigation.The tablets were made in the third phase using a variety of methods, including direct compression and wet granulation.

Granulation in the wet state

Acid Granule Preparation

The acids, namely citric acid and tartaric acid, were mixed with simethecone to make acid granules. For this, simethicone oil was dissolved in methylene chloride and then applied to the sifted acid blend. The moist bulk was sieved at number 20 and the wet granules were removed.Prior to lubrication, the dried granules were passed through mesh no. 16 in a tray drier for about 60 minutes at 53°c+ 2°c to get lod less than 1.0 percent on ir.

Base Granules Preparation

The bases, sodium bicarbonate and sodium carbonate, are granulated with the pvp-k-30 in the manufacture of base granules. To make a transparent solution, the pvp-k-30 was dissolved in methylene chloride. The resultant wet mass was sieved no.20 and dried for about 1 hour at 53°C + 2°C to get a lod of less than 1.0 percent on ir. Prior to lubricating, the dried granules were passed through mesh no. 16.

Granule Lubrication:

The lubricants were combined with a blend of sized base granules and sized acid granules after passing through mesh 40. Water-soluble lubricants were used in the effervescent tablet.The wet granulation procedure was shown to be superior than direct compression in this investigation.

Angle of repose, bulk density, and tapped density were all measured on the granules.

The tablets were tested for thickness, hardness, friability, weight fluctuation, disintegration, active component content, and an in-vitro dissolution study, among other physical criteria. For drug content, disintegration, carbon dioxide, and in-vitro drug release profile, the promising formulations (formula no. f7) were compared to marketed goods.

TABLE N-22 PARACETAMOL(PH -1.2) STANDARD CALIBRATION CURVE

100 mg of paracetamol were precisely weighed and dissolved in 100.0 ml of 0.1n hcl. With 0.1n hcl, 10.0 ml of this stock solution was diluted to 100.0 ml. 10.0 ml of this dilution was further diluted with 0.1 n hcl to make 100.0 ml. Pipette out aliquots of 1.0 ml, 2.0 ml, 3.0 ml, 4.0 ml, 5.0 ml, 6.0 ml, 7.0 ml, 8.0 ml, 9.0 ml, and 10 ml and make up to 10 ml volume with 0.1 n hcl separately. Using a u.v. spectrometer, the absorbance of all of these solutions was measured at 249 nm.

Concentration mcg/ml	absorbance
1	0.021
2	0.042
3	0.063
4	0.085

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5	0.113
6	0.134
7	0.157
8	0.180
9	0.205
10	0.239

Slope=0.0228 r^2 =0.999

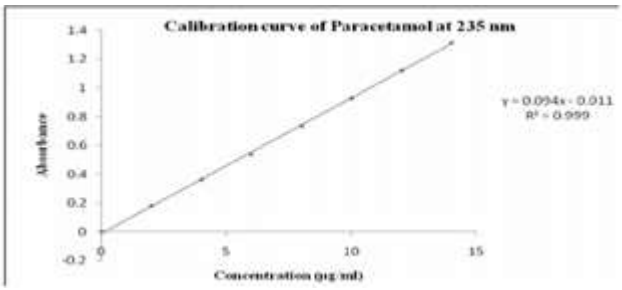


Fig.No.1-Standard Curve Of Paracetamol

Standard curve of Paracetamol

TABLET EVALUATION:

1.TABLET DIMENSIONS: tablet dimensions include tablet thickness and diameter. The mean thickness values obtained from five tablets of each formulation are shown in The number indicates that the die fill was consistent and that the compression force was uniform.

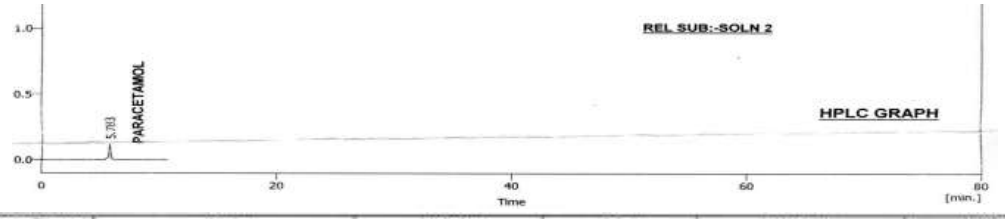
2.FRIABILITY: contains the friability values for each formulation. The values of the preferred formulas are within acceptable limits, showing that these formulations are compact and strong.

3.AVERAGE WEIGHT AND WEIGHT VARIATION: Each formulation was tested with twenty pills.Table no. 1 shows the mean values and weight variation of each formulation. The results show that all of the tablets of various formulations meet the ip/usp standards.

Granule flow ability is shown by the observed narrow range weight variation; desirable packing properties are indicated by the observed narrow range weight variation.and consistent die filling of all formulas The acceptable flow characteristics of granules determined during pre-formulation support this.

4. DISINTEGRATION TIME: For each formulation, a disintegration time test was performed. The findings of each formulation's disintegration time are shown in table no.-. In the final formulation, acids and bases are utilised in 38 percent and 45 percent, respectively.

FIG.NO.2- IDENTIFICATION OF PARACETAMOL BY H.P.L.C.



Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
5.783	694.902	95.962	100.000	100.0	0.12
Total	694.902	95.962	100.000	100.0	

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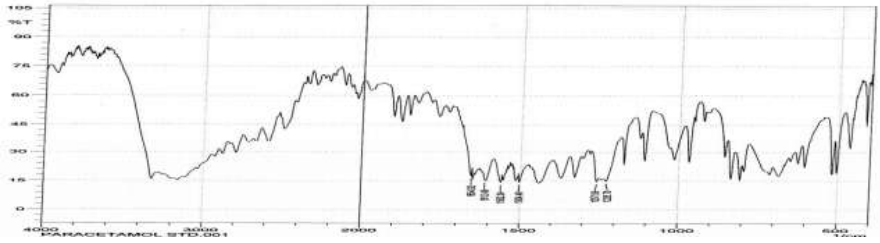
FIG.NO.3-IMPURITY PROFILE OF PARACETAMOL

Result Table - Calculation Method: ESTD

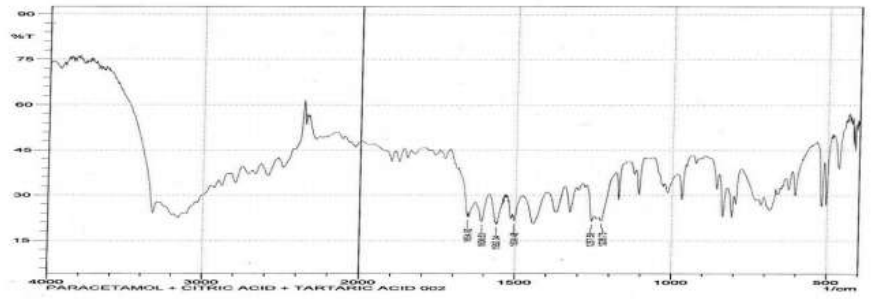
Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
3.860	287.037	39.905	21.221	29.5	0.10
6.070	1065.567	95.458	78.779	70.5	0.15
Total	1352.604	135.363	100.000	100.0	

FIG.NO.4- IR CURVE OF API (PARACETAMOL)



No.	Peak	Intensity	Corr. Inte	Base (H)	Base (L)	Area	Corr. Are
1	1226.73	14.798	5.31	1236.37	1182.36	33.325	0.734
2	1257.59	14.563	5.386	1274.95	1251.8	15.807	0.773
3	1504.48	14.11	4.957	1506.41	1479.4	19.367	0.945
4	1562.34	14.054	1.999	1564.27	1558.48	4.728	0.201
5	1612.49	15.218	1.076	1618.28	1610.56	5.988	0.078
6	1654.92	17.284	6.101	1683.86	1653	16.802	1.251

FIG.NO.5- IR CURVE OF API (PARACETAMOL) + CITRIC ACID + TARTARIC ACID



No.	Peak	Intensity	Corr. Inte	Base (H)	Base (L)	Area	Corr. Are
1	1226.73	21.571	3.935	1236.37	1182.36	28.986	0.233
2	1257.59	21.382	4.966	1274.95	1249.87	14.55	0.634
3	1504.48	21.517	2.316	1506.41	1479.4	15.637	0.024
4	1562.34	20.489	1.272	1585.49	1560.41	14.946	-0.016
5	1608.63	21.32	7.767	1629.85	1585.49	26.116	2.342
6	1654.92	22.862	2.793	1680	1653	13.847	-0.057

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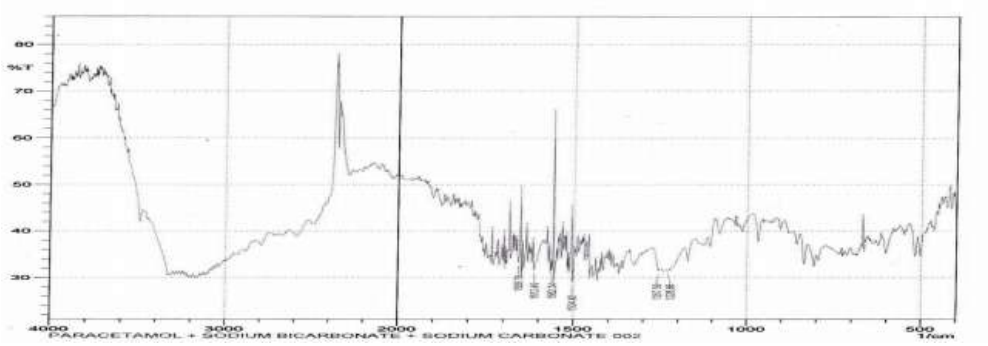
FIG.NO.7- IR CURVE OF API (PARACETAMOL) + SODIUM BICARBONATE + SODIUM CARBONATE



No.	Peak	Intensity	Corr. Inte	Base (H)	Base (L)	Area	Corr. Are
1	1228.66	31.439	0.505	1234.44	1219.01	7.69	0.059
2	1257.59	31.465	1.577	1276.88	1251.8	11.765	0.074
3	1504.48	29.04	14.824	1506.41	1496.76	4.548	0.798
4	1562.34	31.64	12.853	1564.27	1558.48	2.459	0.572
5	1612.49	31.641	4.39	1616.35	1608.63	3.69	0.261
6	1658.78	33.223	10.121	1662.64	1653	4.275	0.845

STABILITY STUDIES:

ACCELERATED STABILITY TESTING:

Because the effervescent tablet's accelerated stability testing period can last up to three months. As a result, it is critical to develop a strategy that would aid in the quick prediction of drug long-term stability.

Accelerated stability testing is defined as a validated approach for predicting product stability by storing the product under settings that accelerate change in a defined and predictable manner.

For one month, prepared pills were tested at 40 degrees Celsius, 76 percent relative humidity, and room temperature. For analysing the stability of the developed formulations, the effects of temperature and time on the physical features of the tablet were investigated. The stability tests were carried out at a room temperature of 20 to 28degrees Celsius. In vitro disintegration time was one of the factors investigated.

TABLES WERE CREATED TO REPRESENT THE RESULTS

TABLE NO 23:- STABILITY PARAMETERS OF FORMULATION F7STORED AT ROOM TEMPERATURE

Parameter	Initial	After 15days	After 30days
Drug content(%)	96%	98.8%	97%

TABLE NO.24. STABILITY STUDY OF IN-VITRO DISSOLUTION FOR FORMULATION F7 AT R.T.

% drug release

Time (min)	Initial	After 15 days	After one months
0	0	0	0
1	105.5	100.25	100.5
2	103.44	99.92	99.45
3	98.25	96.74	94.85
5	99.20	95.25	95.45

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TABLE NO.25 STABILITY PARAMETERS OF FORMULATION F7 STORED AT TEMPERATURE 40^{O}C AND RH 76%.

Parameter	Initial	After 15 days	After one months
Drug content(%)	99%	98.8%	97%
In-vitro disint.time(sec)	70	75	77

TABLE NO.26 STABILITY STUDY OF IN-VITRO DISSOLUTION FOR FORMULATION F7 STORED AT TEMPERATURE 40^{O}C AND RH 76%

Parameter	Initial	After 15 days	After one months
Drug content(%)	05.5%	98%	99%
In-vitro disint.time(sec)	70	75	77

TABLE NO.27 PROPERTIES OF THE PREPARED FORMULATIONS

Property	FD1	FD2	FD3	FD4	FD5	FD6	FD7	FD8	FD9
Thickness(mm)	5.65	5.41	5.51	5.98	5.95	5.90	5.90	5.92	5.94
Disintegration time,seconds	100	90	70	71	76	75	63	65	75
% Compressibility	14.95	32.35	26.79	18.35	20.50	27.70	12.52	14.14	14.14

TABLE NO.28: EFFECT OF ACIDS AND BASES ON EFFERVESCENT TIME OF TABLETS

Property	FD1	FD2	FD3	FD4	FD5	FD6	FD7	FD8	FD9
Bulk density G/CM^3	0.51	0.53	0.53	0.59	0.67	0.67	0.626	0.59	0.59
Tapped density G/CM3	0.589	0.78	0.72	0.72	0.84	0.91	0.7143	0.67	0.67
% Compressibility	14.98	31.58	26.79	18.35	20.50	27.69	12.55	13.20	13.20
Thickness(mm)	5.65	5.40	5.50	5.98	5.95	5.90	5.86	5.89	5.84
Disintegration time(sec)	100	90	70	60	65	75	64	68	73
Water content (i.o.d)%	1.9	1.9	1.9	1.7	3.5	1.5	1.1	1.3	1.5
Diameter(mm)	24.9	24.9	24.9	24.9	24.9	24.9	24.9	24.9	24.9

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TABLE NO. 29 COMPOSITION OF EFFERVESCENT TABLETS OF PARACETAMOL (WET GRANULATION)

Ingredient	FD1	FD2	FD3	FD4	FD5	FD6	FD7	FD8	FD9
Paracetamol	500	500	500	500	500	500	500	500	500
Citric acid (anhydrus)	232.34	105.5	526	521	486	486	495	491	491
Tartaric acid	--	202	1046	1046	983	983	983	971	961
Ascorbic acid	--	--	--	--	--	--	--	--	--
Fumaric acid	191.97	--	--	--	--	--	--	--	--
Sodium bicarbonate	276.85	353.5	1577	1575	1484	1484	1484	1400	1351
Sodium carbonate	--	--	266	266	250	250	251	241	211
Sodium citrate	200	--	21	--	--	--	--	--	--
Sodium benzoate	----	---	---	17	11	15	20	24	29
Mannitol		208	208	208	219	224	--	---	--
Peg-6000	31	20	---	---	25	--	---	--	--
Pvp-k-30	16	17	25	65		60	116	85	100
Simethicone	----	--	-	20	15		65	25	50
Acesulphum potassium	---	--	20	25	20		35	25	20

TABLE NO. 30 COMPOSITION OF EFFERVESCENT TABLETS OF PARACETAMOL (DIRECT COMPRESSION)

Ingredient	FD1	FD2	FD3	FD4	FD5	FD6	FD7	FD8	FD9
Paracetamol	500	500	500	500	500	500	500	500	500
Citric acid (anhydrus)	232.34	105.5	526	521	486	486	495	491	491
Tartaric acid	--	202	1046	1046	983	983	983	971	961
Ascorbic acid	--	--	--	--	--	--	--	--	--
Fumaric acid	191.97	--	--	--	--	--	--	--	--
Sodium bicarbonate	276.85	353.5	1577	1575	1484	1484	1484	1400	1351
Sodium carbonate	--	--	266	266	250	250	251	241	211

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Sodium citrate	200	--	21	--	--	--	--	--	--
Sodium benzoate	----	---	---	17	11	15	20	24	29
Mannitol		208	208	208	219	224	--	---	--
Peg-6000	31	20	---	---	25	--	---	--	--
Pvp-k-30	16	17	25	65		60	116	85	100
Simethicone	----	--	-	20	15		65	25	50
Acesulphum potassium	---	--	20	25	20		35	25	20

TABLE NO.31-COMPARISON OF F7 FORMULATION WITH LEADING MARKETED SAMPLES I.E.ENO FRUIT SALT, HISTAC TABLETS

Property	**FD7**	**MARKTED EFFERVESCENT SALT**	**MARKTED EFFERVESCENT TABLET**
Bulk density(g/cm3)	0.626	07143	0.5883
Tapped density(g/cm3)	07143	07695	0.667
% Compressibility	12.55	6.15	11.65
Hardness(kg/cm3)	4.5	--	5.2
Thickness(mm)	6.85	---	6.62
Disintegration time(sec)	63	30	56
Water content(I.o.d) %	1.1	0.8	0.9
Diameter(mm)	25.8	---	25.5
Co2 content	0.64g/tab(16.35%)	20%	16.25%

III. SUMMARY AND CONCLUSION

In present work we are used different acids and bases in different concentration from that we conclude 1:22 ratio was excellent for this formulation.

pills in were made and tested for solubility, hardness, weight fluctuation, and disintegration time. All of the formulation's hardness and weight variations are within acceptable bounds, however the final formulation's mix of citric acid (20%), sodium bicarbonate (42.5%), potassium carbonate (5.0%), and , the binders PVP-K-30 (2%), sodium benzoate (1 %). as a result of these components' good effervescent reaction and lack of sticking or capping issues compared to other formulations.

The best effervescence is achieved by using citric acid (20%), sodium bicarbonate (42.5%), potassium carbonate (5.0%), and pvp-k-30 (2%) in the formulation of the effervescent

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tablets of paracetamol and ibuprofen for quick analgesic, anti-pyretic action, and anti-inflammatory action. The binding agent employed was ethanol. One percent sodium benzoate is used as a lubricant.

The effervescent pills were made by wet granulation utilising several binding agents, such as mannitol, ethanol, peg6000, and pvp-k-30 (also act as lubricant).When peg-6000 were used as the binding agent, the solution time was shorter than when pvp-k-30 and ethanol were used, and the produced tablets were assessed for content uniformity and physical properties.Within 2 min. 50 sec., every FDT that was prepared crumbled.The paracetamol quickly dissolved in every FDT that was created. In each instance, the concentration of superdisintegrant increased along with the rate of paracetamol dissolution.

The goal of the research was to develop an effervescent analgesic and antipyretic pill (paracetamol). The literature research revealed that paracetamol has a similar mode of action to aspirin due to structural similarities. By blocking the cyclo-oxygenase enzyme, paracetamol reduces the formation of prostaglandins, which are implicated in the pain and fever processes.Using various acids and bases, an attempt has been made to manufacture an effervescent tablet containing immediate release of paracetamol in this study. At this project, we employed various acids and bases in various concentrations.

1.Compatibility testing was done in the preformulation research, which means that the medicine, acids, bases, and other excipients are all compatible.

2.Wet granulation and dry granulation were both used in the tablet formulation.Wet granulation was used in that procedure, and it was proven to be acceptable.

Various evaluation studies were conducted on all of the formulations. The outcome of granule testing and tablet size, hardness, friability, and weight changes.

The water content of an effervescent tablet can be determined using the Karl Fischer titration method. The carbon dioxide level of the effervescent pills is also a factor.

• Tablet dimensions uniformity means that die fill was consistent and compression force was constant.

• Tablets with high hardness levels have superior mechanical strength and handling properties.

• Formulation compactness is determined by friability values.

• The weight variation of all formed tablets was acceptable, owing to good granule flow characteristics.

The active component content homogeneity of all formulations is within acceptable limits, ensuring dose uniformity.

• In assessment studies, the promising formulation F7 was discovered.

Different acids and bases, as well as their combinations in various quantities, were used to make the placebo tablets. The hardness, disintegration time, weight variation, and solubility of the nine placebo tablets were all tested. The final formulation, which contains a mixture of citric acid (12.56 percent), tartaric acid (25.17 percent), sodium bicarbonate (38.20 percent), sodium carbonate (6.41 percent), and the binding agent PVP-K-30 (2.94 percent) and sodium benzoate, has a hardness and weight variation within limits (0.52 percent). Because these chemicals have a good effervescent reaction and don't have the same capping and sticking issues as other formulations, they're a smart choice.

Different acids, such as citric acid, tartaric acid, fumaric acid, and ascorbic acid, can be used to make the effervescent tablet in various concentrations. Various lubricants and binding agents are also employed in this process. Citric acid, tartaric acid, sodium bicarbonate, and sodium carbonate are found in seven different formulations.

All of the formulations were examined for hardness, friability, weight variation, effervescent time, and other factors. All of the formulations were found to be effervescent for up to 72 seconds. However, the formula contains 12.56 percent citric acid, 25.17 percent tartaric acid, 38.20 percent sodium bicarbonate, and sodium carbonate (2.94 percent). As a result, these acid and base concentrations were used in the final formulation.The effervescent tablet was made using a variety of methods, including direct compression and wet granulation. The content homogeneity and physical properties of the produced tablets were assessed. It was discovered that there was a capping issue with direct compression. As a result, the top surface of the tablets is not correctly set. However, with the help of wet granulation, the powder becomes free flowing, and the compression of the tablets is much better than with direct compression. The rationale for choosing wet granulation is that with dry granulation, capping and sticking problems emerge. nonetheless, wet granulation In comparison to direct compression, the granules develop good flowing qualities with this approach. Wet

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granulation protects acids and bases from moisture in the environment. The problem of capping was also reduced. The humidity and temperature must be precisely regulated throughout the production of effervescent tablets. The tablet should have an L.O.D. of less than 1%. Because if the effervescent pill contains only one water molecule, the effervescent reaction achieved should be minimal.The stability study, also known as an accelerated stability study, can be carried out at 400 degrees Celsius and 75% relative humidity according to I.C.H. criteria. The stability test can also be done at R.T, 45°C, and at a cold temperature of 2-5°C. For the above-mentioned parameters, the formulation showed no significant fluctuations and remained stable over the required time period. The effervescent tablets of paracetamol can be manufactured for fast analgesic and antipyretic action using citric acid (12.56 percent), tartaric acid (25.17 percent), sodium bicarbonate (38.20 percent), and sodium carbonate, according to the preceding summary (2.94 percent). delivers a more effervescent result The binding agent employed was PVP-K-30. As a lubricant, sodium benzoate (0.5%) is used.

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