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Formulation And Evaluation Of Effervescent Garnules Using Lemon Leaves And Ajwain Extact

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ABSTRACT:
The main purpose of this research was to formulate and evaluate the effervescent granules of lemon leaves and ajwain extract by wet granulation method. According to the observations of this research, the effervescent granules overcomes the 5 benefits than the regular liquid dosage form like pleasant taste compared to regular tablets, distributed more evenly, increased liquid intake, easy alternative to regular tablets, easy alternative to regular tablets as well as it increases the absorption, stability, quicker and prolong the onset of action with antioxidant and antacid activity.
As per the formulated evaluation were different parameters like bulk density (0.52), tapped density (0.68), angle of repose (30.5), carr's index (23.5), hausner's ratio (1.30), effervescence time (30-50 sec), its shows green in colour, characteristics in odour and amorphous granular appearance.

INTRODUCTION

Effervescent granules are granular dosage form of drug in a dry mixture usually composed of effervescent like sodium bicarbonate, citric acid and tartaric acid. Effervescent granules when added to water, the acids and the base react to liberate CO2, resulting in effervescence. The bitter taste of the drug can be masked by the effervescence that was produced when the formulation is mixed with water. Effervescent granules are the granular dosage forms having drug and effervescent base 1 which is composed of sodium bicarbonate, citric acid and tartaric acid, when added to water, the acids and the base react to liberate CO2, resulting in effervescence. Effervescent granules form attractive dosage form as the carbonated solution masks the undesirable taste of the drug.[4]
Granules are a type of dosage form and composed of dry aggregates of powder particles that may contain one or more APIs, with or without other ingredients. Granules are frequently compacted into tablets or filled into capsules, with or without additional ingredients. Effervescence is the escape of gas from an aqueous solution and the foaming or fizzing those results in the release. Effervescent granules are popular delivery systems due to their fast dissolving, highly soluble, and stable nature. Nowadays, many pharmaceutical products such as antacids, analgesics, and cough/cold are dispensed as effervescent granules. The dosage form is dissolved or dispersed in water to initiate the effervescence before ingestion [4-7]. The advantages of effervescent granules are easy to administer, onset of action is faster, easily portable, gentle on the digestive tract, it is better tasting, and more stable than liquid dosage form. With advantages, there have some disadvantages also these are – cannot be given to the children due to the possibility of gas (CO2) toxicity. If the packaging is not done properly, then there are chances of degradation by environmental moisture. It has a shorter shelf life as compared to other solid dosage forms.[5]
Ascorbic acid (vitamin C) is a water-soluble vitamin and possesses a potent antioxidant activity. Vitamin C presents naturally in Citrus and most of fruits and vegetables. It has many functions like protects against respiratory tract infections and reduces risk for cardiovascular diseases and even Cancer. Effervescent granules are one of the solid dosage forms that is taken orally, and noticeably the effervescent preparations are becoming increasingly due to many advantages such as good stability, quickly dissolve, masking of unpleasant taste and ease administration with highly compliance in patients with difficulty in swallowing of pills and tablets, moreover the bioavailability of low absorbed drugs can be increased. However, the disadvantages are needing controlled preparation and packaging area to protect from moisture and light that makes the medicine more expensive. The major of effervescent products are analgesics, antacids, supplements and flu-cough formulations.[6] The oral dosage forms are the most popular way of taking medication despite having some disadvantages like slow absorption and thus onset of action is prolonged. This can be overcome by administrating the drug in liquid from but, many APIs have limited level of stability in liquid form. So,

effervescent tablets act as an alternative dosage form. The tablet is added into a glass of water just before administration and the drug solution or dispersion is to be drunk immediately.[7]

Figure 1

Here we look at 5 benefits of effervescent tablets over regular tablets.[9]

1. Pleasant Taste Compared to Regular Tablets

Effervescent tablets are so popular due to the fact they can be dissolved in a liquid such as water or fruit juice, meaning that they often taste better than regular tablets. Conventional tablets dissolve slowly which can result in reduced absorption rates, effervescent tablets, in contrast, dissolve quickly and completely, meaning you get the full benefit from the ingredients.

2. Distributed More Evenly

Conventional tablets dissolve gradually in the stomach once ingested and can sometimes only partially dissolve which can lead to irritation in some cases. The benefit of effervescent tablets is that they dissolve completely and evenly meaning that localized concentrations of the ingredients cannot occur. This means not only a better taste but also less chance of irritation and a more efficient means of ingesting the ingredients.

3. Increased Liquid Intake

Effervescent tablets provide the nutritional benefits intended, but in addition to this they also increase liquid intake. This can be especially beneficial if you are dehydrated or ill and not ingesting as much fluid as usual. Effervescent tablets can be a fantastic way of rehydrating as well as reaping the benefits you are taking the tablets for whether this is a dietary supplement, herbal or medicinally.

4. Easy Alternative to Regular Tablets

They can be a great alternative for those who may have trouble swallowing either due to illness or age. Older individuals may have difficulty swallowing but need to take medication or supplements on a regular basis and in this respect, effervescent tablets can be a lot easier than having to swallow a tablet. In addition to this, they can be a great way of ingesting medicine for individuals with sore throats or medical issues that make swallowing difficult and so are a viable alternative to regular tablets.

5. Simple and Easy to Measure

Effervescent tablets are easily dissolved into water or a liquid of your choice and then after a while are consistent, well mixed and ready to drink. Traditional tablets or powders, however, need to be measured and stirred in repeatedly to avoid an inconsistent drink with lumpy bits.

Even with stirring and measuring it is common to have an inconsistent drink with lumpy bits and an odd taste and this is where effervescent tablets are more efficient. Simply drop them in and they dissolve fully and evenly ensuring you get all the benefits of the tablet, as well as being able to comfortably drink it.

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1. To Sum Up

Effervescent tablets are becoming increasingly popular and it is easy to see why. They provide a much more efficient way of taking supplements or medication due to being distributed evenly and much more quickly than regular tablets. In addition to this, they taste better as can be added to water or a liquid drink of your choice as well as being easier to take for people who may find it difficult to swallow.[9]

A.Mechanism of Effervescence:

$C_6H_8O_7.H_2O + 3NaHCO_3 (aq) \rightarrow Na_3C_6H_5O_7 + 4H_2O + 3CO_2 (g) \uparrow$
Citric acid + Sodium bicarbonate → Sodium citrate + Water + Carbon dioxide

$C_4H_6O_6 + 2\ NaHCO_3 \rightarrow Na_2C_4H_4O_6 + 2H_2O + 2CO_2 (g) \uparrow$
Tartaric acid + Sodium bicarbonate → Sodium tartrate + Water + Carbon dioxide

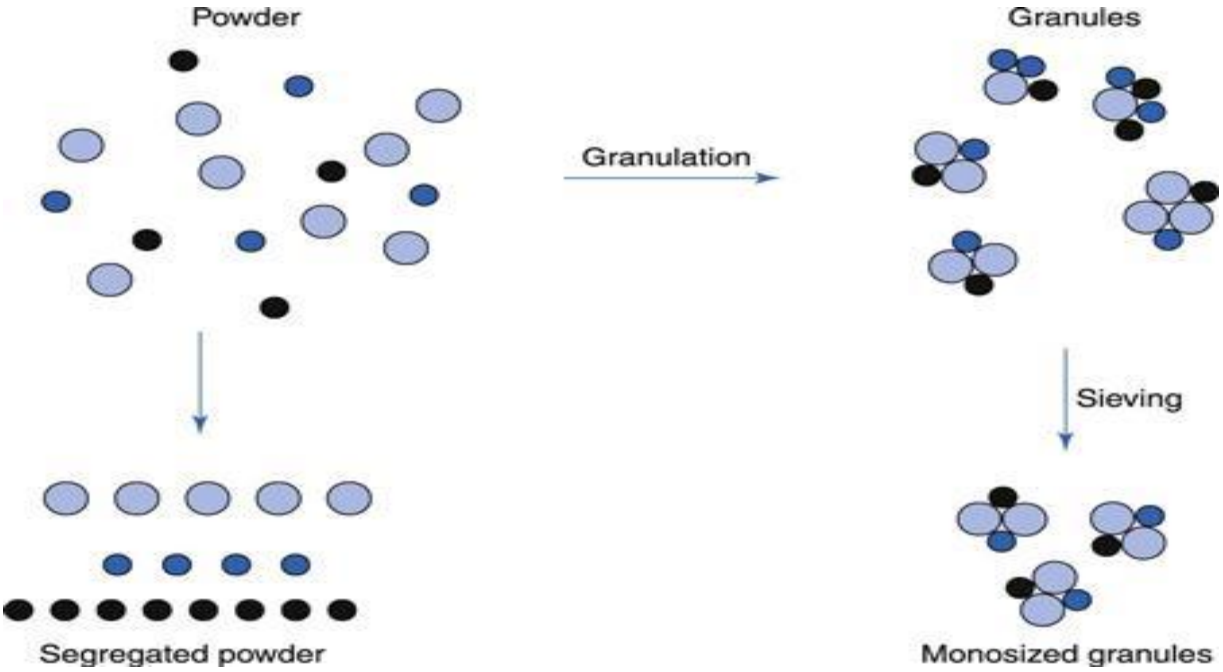

Figure 2

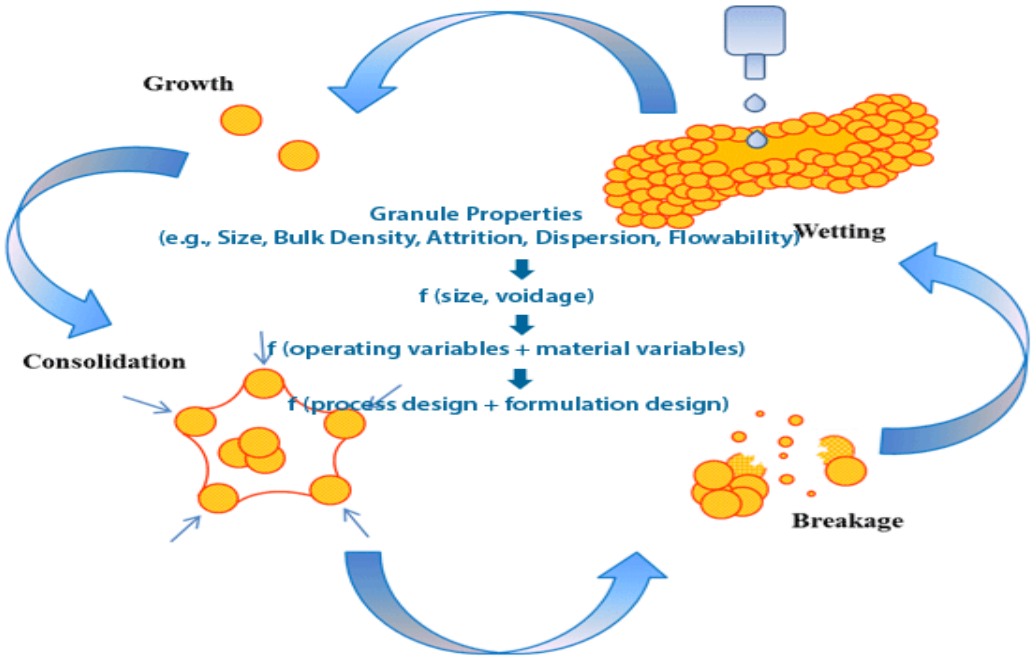

Figure 3

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B.Fundamentals of Effervescent

The choice of ingredients for effervescent granules depends mainly on two aspects:
Requirement of the manufacturing process & the requirement of constructing a preparation which dissolves in water.
Acids: Samples of such acids include Citric acid, Tartaric acid, Malic acid, Adipic acid and Fumaric acid.
Bases: Samples of bases include Sodium carbonate, Sodium hydrogen carbonate, Potassium bicarbonate, Sodium sesquicarbonate [20]

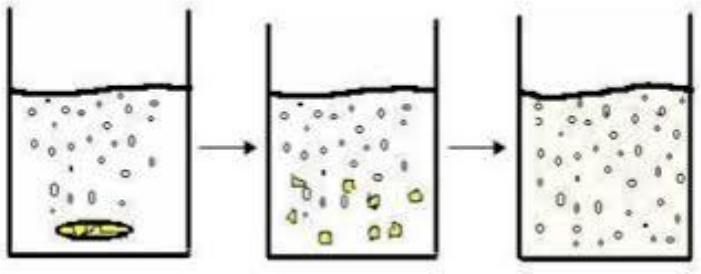

Figure 4

C.Effervescent Granules preparation

There are various methods of preparation of effervescent granules viz.
Wet Method, hot melt extrusion technique, Dry Method or Fusion method & non aqueous method.

1. Hot Melt Extrusion Technique

Firstly, weigh the required quantity of ingredients and pass them through sieve no 18. Heat it a temperature of about 50 0C to 80 0C until a molten mass is obtained.Now cool down the mass at room temperature and then pass the mass through the sieve no8 or sieve no10 to obtain granules.Finally dry the granules at a temperature not exceeding 60 ºC.29-30

2.Fusion Method or Dry Method

It is the most important method for the preparation of effervescent granules. In this fusion method compression step is eliminated. In this method the powders are heated using an oven or source of heat. Fusion method uses the water of crystallization present in the citric acids which acts as binding agent. The powdered mixture is stirred well to obtain a uniform mass and is passed through a sieve to obtain granules and is finally dried in an oven.

3.Wet Method

It is the oldest method of granule preparation. Firstly, all the ingredients are powdered and are gone through a sieve to induce uniform particle size. Wet massing is the most significant step within the wet granulation process. During this step to the powdered mixture a granulating agent is added. After the powdered mixture is moistened it is passed through a mesh screen to produce desired size granules. Later these granules are dried by using a hot air oven.

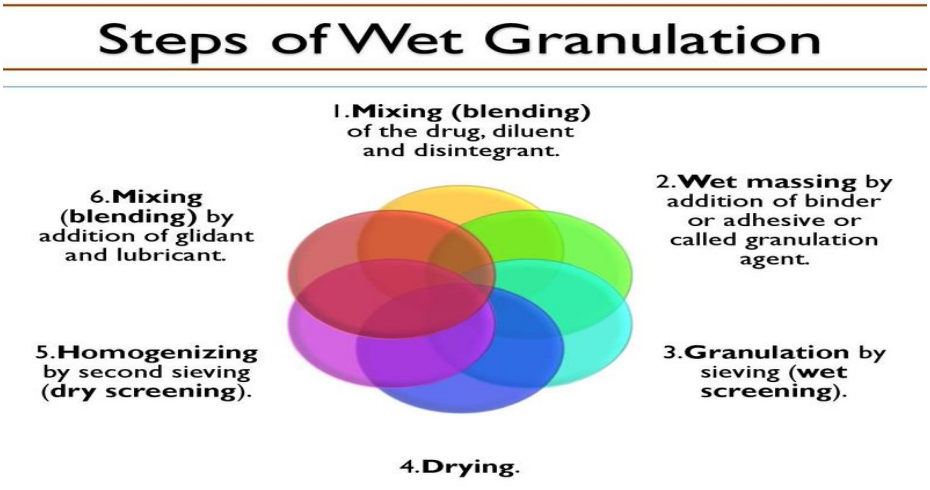

Figure 5

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4.Non-Aqueous Method

The ingredients are weighed and are taken into a china dish. To the ingredients add drop by drop alcohol (Ethanol) until it forms a mold. Pass the mold through the sieve no 10, granules are obtained & these granules are kept in an oven at temperature of 55o C for 12 hrs, The granules are again passed through the sieve to obtain uniform sized granules. These granules are further packed in Sachets and are stored for further use.

Effervescence consists of a soluble organic acid and an alkali metal carbonate salt, one of which is often the API. Carbon dioxide is formed if this mixture comes into contact with water. Typical examples of the acids and alkalis used include: Citric acid, Tartaric acid, Malic acid, Fumaric acid, Adipic acid, Sodium bicarbonate, Sodium carbonate, Sodium sesquicarbonate, Potassium bicarbonate, Potassium carbonate.[20] A tiny evergreen tree from Asia, is known as *Citrus limon* (lemon). The lemon has a number of different species and has yellow ellipsoidal fruit. It is the most important species after oranges and mandarins of citrus fruit.[8] Citrus have a strong commercial value. They are produced mainly for the fresh consumption, but they are also addressed to the food industry for the production of fruit juice. Moreover, the byproducts generated following their industrial process are source of important bioactive compounds with potential for animal feed, manufactured foods and health care. Among the citrus byproducts, EOs have been produced for more than a thousand years. The main producing countries are Italy (particularly Sicily), USA (Florida) and South America (Brazil, Argentina). The fruit of citrus is a hesperidium, a type of berry with a pericarp (divided in exocarp or flavedo, mesocarp or albedo and endocarp) and segment, filled with juice sacs (vesicles), actually specialized hair cells. Approximately 50% of the citrus fruit weight consists of pulp, seeds and peel, which can be processed into value-added byproducts such as molasses, pectins, fiber, seed oils, fermentation products and Eos. In all citrus species of the *Rutaceae* family, essence of oil secretory cavities (glands) has been reported.[11]

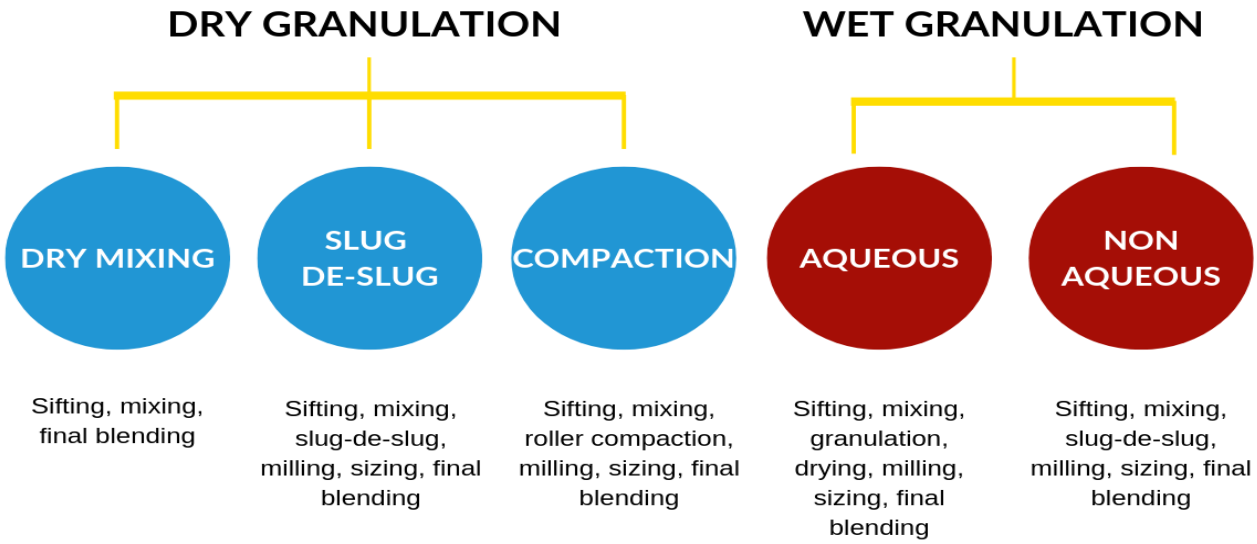

Figure 6

Figure 7

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DRUG PROFILE
1.Lemon leaves
Kingdom – Plantae
Order – Sapindales
Family – Rutaceae
Genus – Citrus
Species – C. limon
Synonym - citrus fruit leaves

Biological source- Small evergreen tree in
flowering plant
Chemical constituent - limonene (69.9%), β-pinene (11.2%), γ-terpinene (8.21%), (Figure 4), sabinene (3.9%), myrcene (3.1%), geranial (E-citral, 2.9%), neral (Z-citral, 1.5%), linalool (1.41%).
Activity – Antioxidant, Antitumor, Antimicrobial.

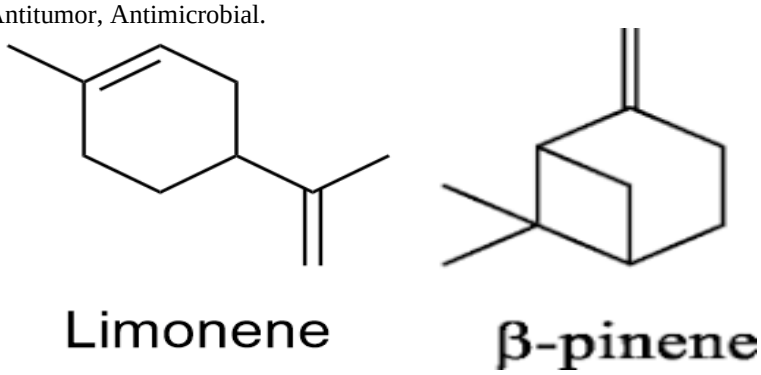

Figure 8

1. Ajwain
Kingdom – plantae
Order – apiales
Family – Apiaceae
Genus – Trachyspermum
Species – T. ammi
Synonym - Ajowan, Trachyspermum ammi
Biological source - Dried ripe seeds of Trachyspermum ammi (L.) Sprague.
Chemical constituent - Thymol (39.1%) followed by oleic acid (10.4%), linoleic acid (9.6%), gamma-terpinene (2.6%), p-cymene (1.6%), palmitic acid (1.6%), and xylene (0.1%).

Activity – Antioxidant, Antimicrobial, Antifilarial, kidney stone inhibitory.

Figure 9

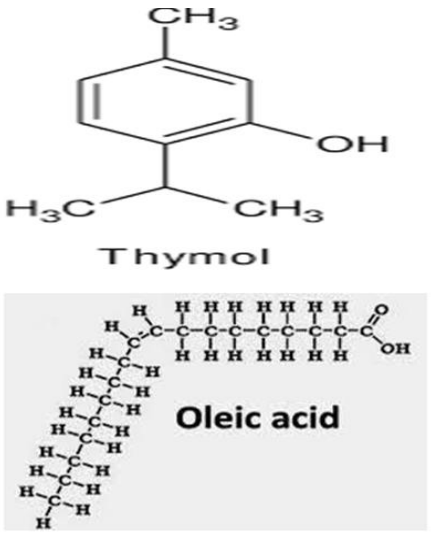

Figure 10

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MATERIAL AND METHOD

Material –

Sr. No.	Chemicals	Quantity
1	Sodium Bicarbonate	10gm
2	Sodium Carbonate	10gm
3	Anhydrous citric acid	10gm
4	Lemon leaves powder	7gm
5	Ajwain powder	7gm
6	Water	QS

Table 1

Method of Preparation –

Wet method - The wet method differs from the fusion method in that the source of binding agent is not the water of crystallization from the citric acid but ethanol was used as the moistening agent, forming the pliable mass for granulation. In this method, all of the powders (anhydrous) were weighed and placed in a mortar, and then, ethanol was added drop by drop until we get a wet mass to pass the ball test. Then, the wet mass was sieved and the granules were dried in an oven at temperature 40°C for 10 min; then, the granules were placed in container and tightly sealed.

Figure 11

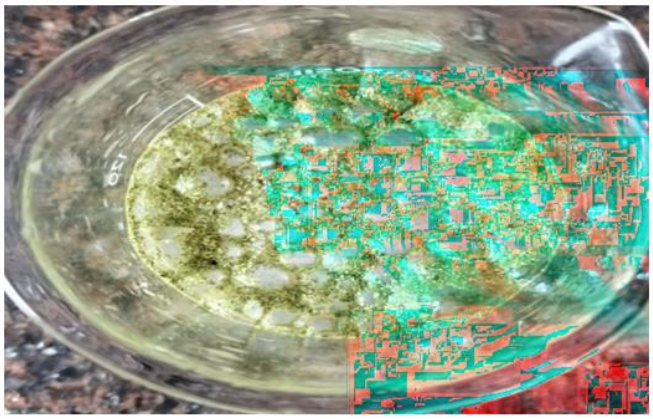

Figure 12

EVALUATION OF EFFERVESCENT GRANULES -

[1] Angle of repose

The prepared granules were allowed to pass through a funnel and the height of the pile (h) and radius of the pile (r) are measured. From this, the angle of repose, i.e., the angle between the height of the pile and radius of the pile is calculated with the help of the following formula.

Tan Θ = h/r

Θ = tan-1(h/r),

Here, h= height of the powder pile,

r = radius of the powder pile

TYPE OF COHESION	MEASURE OF ANGLE OF REPOSE
Very low Cohesion	Less than 30°
Low Cohesion	30 to 38°
Passable	38 to 45°
Cohesive	45 to 55°

Table 2

[2] Bulk density

A certain quantity of granules was taken in a measuring cylinder without compacting. The proper level of Granules was maintained, the volume V1 (bulk volume) was measured and calculated according to the formula given below:

Bulk density = Weight of the granules / V1

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[3] Tapped density
A certain number of granules was taken and tapped for 100 times in a measuring cylinder. Then the tapped volume (V2) is measured and calculated according to the formula given below:
Tapped density = Weight of the granules / V2

[4] Carr's Index
Carr's Index is determined by using a formula44
Carr's index ratio = [(Tapped density–Bulk density)/Tapped density] × 100

Compressibility index	Observation
≤10	Excellent
11-15	Good
16 – 20	Fair
21 – 25	Passable
26 – 31	Poor
32 – 37	Very Poor
>38	Very Very Poor

Table 3

[5] Hausner's Ratio
Flow property of the powder can be determined using the Hausner's ratio. Lower the Hausner ratio betters the flow property or vice versa. Hausner's ratio is calculated by the formula.
Hausner's Ratio = Tapped density/Bulk density

[6] Effervescence Time
In vitro effervescence time was measured by dissolving some quantity of the granules in a beaker containing 50ml of Water. Granules were randomly selected from the batch.

Figure 13

RESULT AND DISCUSSION

The prepared antioxidant effervescent granules show antioxidant and antacid activity. Bulk density of granules was found to be 0.52, angle of repose 30.5, tapped density 0.68, carr's index 23.5, hausner's ratio 1.30, effervescence time 30-50 sec, green colour, characteristics odour of lemon, ajwain, having amorphous granular appearance.

Sr. No.	Evaluation Parameters	Observation
1	Angle of repose	30.5
2	Bulk density	0.52
3	Tapped density	0.68
4	Carr's index	23.5
5	Hausner ratio	1.30
6	Effervescence time	30 – 50 sec
7	Colour	Green
8	Odour	Characteristics
9	Appearance	Amorphous granules

CONCLUSION

Antioxidant effervescent granules using lemon leaves and ajwain were prepared successfully by wet granulation method containing sodium bicarbonate, sodium carbonate, anhydrous, citric acid and granulating agent ethanol. Formulated granules had given satisfactory results of various parameters like angle of repose, bulk density, tapped density, carr's index, hausner's ratio, effervescence time, colour, odour, appearance etc.

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