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DEVELOPMENT AND EVALUATION OF ANTI-OBESITY POLY HERBAL GRANULES

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ABSTRACT

The current study's in-vitro anti-obesity efficacy is focused on the formulation creation and assessment of effervescent granules manufactured using a herbal extract mixture (a combination of raw Coffee arabica L. beans, Achyranthes aspera seeds, and hydro-alcoholic extract of Garcinia indica fruits). The soxhlet extraction method was used to extract all 3 plant components hydro-alcoholically. The bulk density, tap density, car's index, hausner's ratio, angle of repose, and length of the effervescent cessation were all measured and evaluated for the effervescent granules. The physical characteristics of each batch were satisfactory. Additionally, the in- vitro lipase and α-amylase inhibitory activities of the herbal extract combination were examined at different concentrations (50, 100, 150, 200, 250, and 300) µg/ml. The herbal extract mixture had the highest inhibitory action against lipase and amylase at a concentration of 300 µg/ml, exhibiting 83.32± 10.47 and 69.14± 7.22, respectively. The results of this study might be useful in the future for formulating effervescent products made using plant extracts.

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Keywords: *Amylase, Pancreatic lipase, Effervescent granules, Herbal extract mixture*

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INTRODUCTION

Being overweight is the fifth largest cause of mortality globally and is considered a serious public health concern[.[1] One According to medical definitions, obesity is the condition in which a person has gained so much extra body fat that it may have a detrimental effect on their health, possibly leading to a lower life expectancy and/or more health problems.[2] Two Being overweight or obese is not just a cosmetic problem; it is also associated with several other lifestyle conditions such as diabetes, cancer, dyslipidemia, cardiovascular disease, hypertension, and musculoskeletal problems.[3]

Herbal medicine combines a variety of bioactive compounds to cure imbalance and enhance health, in contrast to mainstream medicine, which frequently focuses on a single pathway or symptom.[4] Achyranthes aspera is a notable perennial medicinal herb that belongs to the Amaranthaceous family and is a weed. The roots, seeds, and shoots of this plant have been shown to have therapeutic properties by the conventional medical system. Pharmacological activity, including hepatoprotective, diuretic, laxative, purgative, anti-allergic, and anti-asthmatic properties, have been reported for many isolated phytochemical components. Many skin ailments, including as scabies, snake bites, asthma, cough, dropsy, ulcers, piles, and rheumatism, have long been treated using the herb.[5] Five seeds contain saponins A and B. It has been demonstrated that Achyranthes aspera seeds have antiobesity qualities by modifying the blood lipid profile and avoiding the excessive development of fat.

Known by its dried rind as "kokum," Garcinia indica is a tropical fruit with a pleasant, tangy-sweet taste and a plethora of health advantages. It is regarded as a wonder berry.[6] For a very long time, kokum has been used in herbal medicines for conditions including rheumatism, diarrhea, constipation, inflammatory diseases, and excessive sweating.[7] The juice of the kokum rind is used to cure colic, diarrhea, and dysentery. Kokum fruit contains the highly valued anti-obesity chemical hydroxy citric acid. In addition, fruits include citric acid, oxalic acid, garcinol, isogarcinol, xanthochymol, and isoxanthochymol. The mammalian system employs hydroxyl citric acid as a potent biochemical control of obesity and lipid disorders, as was recently revealed.[8]

One of the most often consumed traditional coffee varieties is green coffee extract (GCE), which is produced from unprocessed (unroasted) or green coffee beans.Green coffee has twelve different nutrients: theophylline, trigonelline, theobromine that chlorogenic acid, which is a protein, lipids, and minerals. Green coffee contains both chlorogenic acid and caffeine, which are thought to provide a number of health benefits, including anti-inflammatory properties, tumor fighting, anti-diabetic, anti-hypertensive, and anti-obesity qualities.[9]

Oral administration is considered the most effective medication delivery strategy with the best percentage of patient compliance. The medicinal agent, which is usually a dry combination of acids such as citric acid, tartaric acid, and bicarbonate of sodium, is the main component of effervescent granules.[10] When bases and acids react with water to release carbon dioxide, effervescence is created. The resultant carbonated fluid usually masks the unpleasant taste of the drug.[11] Since an effervescent vehicle dissolves granules in solution quickly, it may be able to improve the flavour and palatability of the final solution, which is needed because the decoction product isn't delicious enough. This product comes in a variety of Flavors and has sweetener, which might improve patient compliance—especially for expecting mothers—with their medicine. Nineteen During the small intestine's absorption phase, the enzyme known as pancreatic lipase hydrolyses dietary lipids into free fatty acids.[12]

On the other hand, simple sugars are produced when amylase enzymes hydrolyse carbohydrates during the absorption process in the small intestine.[13]

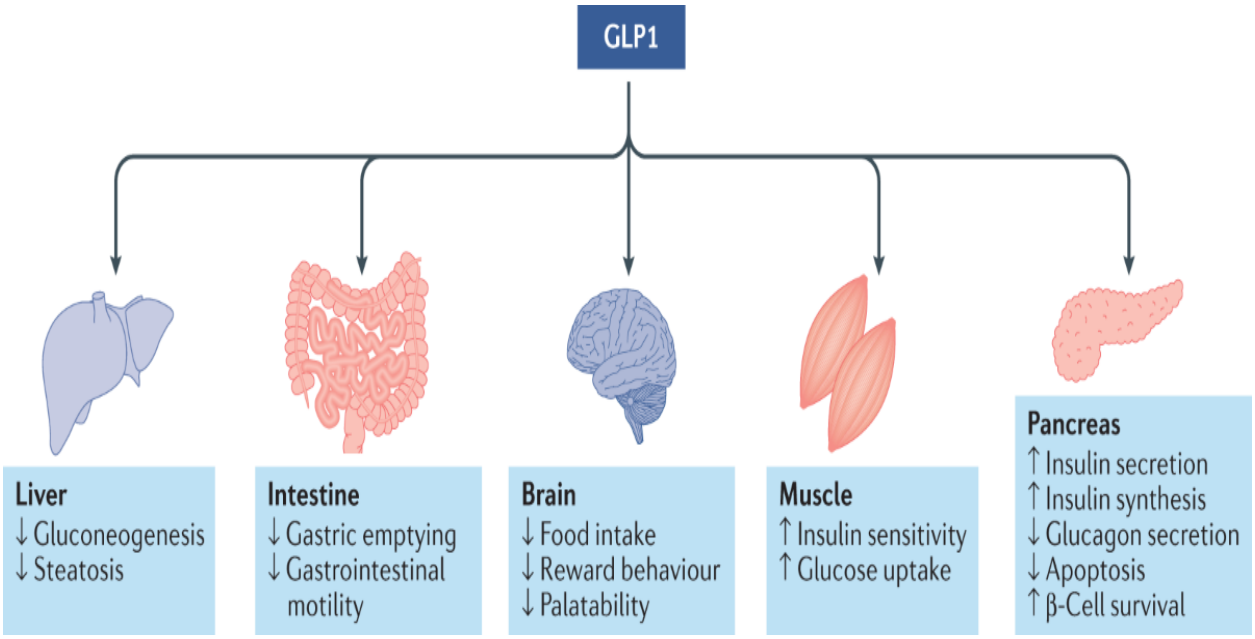

Figure No.1: GLP1 action on various body organs

Collection and identification of plant material

The development of anti-obesity polyherbal granules involves a multi-phase plan to ensure efficacy, safety, and market readiness. Initially, extensive research is conducted to identify and select medicinal herbs known for their anti-obesity properties, such as Garcinia cambogia, Commiphora mukul, and Green tea extract.[14,15,16] The selected herbs undergo phytochemical screening to identify active compounds. Following this, the formulation phase involves determining the optimal ratio of these herbal extracts to maximize synergistic effects. Granules are prepared using appropriate binders and excipients, ensuring stability and bioavailability.[17] The evaluation phase includes in vitro and in vivo studies to assess the anti-obesity potential, focusing on parameters like lipid profile modulation, appetite suppression, and metabolic rate enhancement. Toxicological studies ensure the safety profile of the formulation. Clinical trials on human subjects further validate efficacy and safety, comparing the results with existing anti-obesity treatments. Post-trial, the product undergoes standardization and quality control checks to maintain consistency. Finally, the product is prepared for commercialization, including packaging, marketing strategies, and regulatory compliance to meet the standards set by health authorities. The comprehensive plan ensures that the polyherbal granules are effective, safe, and ready for market introduction, offering a natural alternative for obesity Management.[18]

Materials

List all of the active pharmaceutical ingredients (APIs) that were utilised, along with the sources and purity of each one.

For instance, K Patel Suppliers provided the Garcinia Cambogia extract (95% HCA). List all of the excipients along with their sources and roles.For instance, microcrystalline cellulose from ABC Chemicals was used as a binder and lactose monohydrate as a filler.[19]

Granulation Agents: List all granulating agents that were applied. For instance, DEF Chemicals sells polyvinylpyrrolidone (PVP) K30.

Equipment

Enumerate the apparatus utilised for drying, mixing, granulating, and any additional procedures. For instance, a fluid bed dryer, a high-shear granulator, etc.

Methodology

Studies before formulation

Analyze Solubility: Find out which solvents the active ingredients are soluble in. Utilizing Differential Scanning Calorimetry (DSC) or Fourier transform infrared spectroscopy (FTIR), conduct tests to ascertain the compatibility of active components and excipients.

Granulation Method: Explain the procedure of combining granulating agents and active ingredients to form granules, known as "wet granulation.

Example

To combine the excipients and active ingredients, a high-shear granulator was employed. PVP K30 dissolved in distilled water was used for granulation.

Drying: Describe how the granules will be dried. Example: For two hours, the wet granules were dried at 60°C in a fluid bed dryer.[20]

Flow characteristics: assess the granules' flow characteristics. An illustration would be the measurement of the angle of repose, bulk density, tapped density, and Carr's index.

Experimental work

Procedure for preparation of Effervescent Granules

The following ingredients were precisely weighed

sodium phosphate, citric acid, tartaric acid, and sodium bicarbonate.

All of the materials were mixed in ascending weight order using a trituration technique.

A water bath was used to heat a porcelain dish until it boiled. The powder mixture was added to the hot porcelain dish, which was submerged in a bath of boiling water.

A spatula was used to stir the powder mixture for one to five minutes, or until a damp, cohesive mass formed.

After placing the moist mass on butter paper, it was quickly put through the sieve. Granules were spread out on paper, dried in a hot air oven set no higher than 60°C, and then sealed tightly in an airtight container.[21]

Formulation Table

Ingredients	Batch 1	Batch 2	Batch 3	Batch 4	Batch 5	Batch 6
Extract a mixture (0.5gm)	1.5	1.5	1.5	1.5	1.5	1.5
Citric acid (gm)	2	2.5	2.5	2	2	2.5
Tartaric Acid (gm)	2.5	2.5	3.5	3.5	3	2
Sodium Bicarbonate (gm)	5	4	3.5	4	4.5	5
Aspartame (gm)	0.5	0.5	0.5	0.5	0.5	0.5
PEG600 (ml)	0.5	0.5	0.5	0.5	0.5	0.5
Lemon oil (ml)	0.5	-	0.5	-	0.5	-
Peppermint oil (ml)	-	0.5	-	0.5	-	0.5

Table No.1: Formulation of effervescent granules

Assessment of Herbal Effervescent Granules Formulated

The prepared herbal granules were assessed using a range of assessment criteria.

Angle of repose

The flow characteristics of solids have been described using the degree of repose. One characteristic of inter-particulate the friction or the resistance to particle movement, is the angle of repose.

$\text{Tan}(\theta) = h/r$

The stable, three-dimensional angle that a material pile in the shape of a cone takes during its creation is known as the angle of repose. The funnel approach was used to calculate the degree of repose. The maximum cone height (h) was attained by pouring the liquid via a vertically adjustable funnel. It was computed what the heap's radius and angle of repose were. It is the angle formed by the pile's base and heap. A lower angle of repose indicates better flowability, which is favourable for processes like mixing and packaging.[22]

Bulk Density

Mass density Numerous gaps exist between particles when they are not tightly packed. In light of this, powder's bulk volume increases. The bulk volume of a powder determines its classification as "light" or "heavy." The powder's bulk volume is low because smaller particles sift in between the larger ones. Heavy powders are what these powders are known by. Particle shape, cohesiveness, and size distribution all affect bulk density. Using a graduated measuring cylinder, the bulk density apparatus was filled with the granule blend to determine the bulk density. The measurement of the granule's initial volume is made. This is the volume in bulk. The following equation is used to calculate bulk density. Powder weight divided by bulk volume equals bulk density (Pb).

Deduct the weight of the graduated cylinder when it is empty from the weights of the full cylinder to Determine the mass of the herbal granules:

Weight of herbal granules=$W2-W1$

Weight of herbal granules=W2−W1

Calculate the bulk density (ρ) using the formula:

$$D=M/V$$

where bulk density is expressed in grams every milliliter (g/mL) and weight is expressed in grams (g) with volume in millilitres (mL). [22]

True Density: -

Density is influenced by the type of molecules, their arrangement within the sample, and the position of atoms inside those molecules. Bulk density is another property of powder that distinguishes it from true density. The measurement does not account for the volume filled with voids (inter-particle spaces) and intraparticle pores. The bulk density apparatus, liquid displacement, and helium or nitrogen displacement are used to determine the true density. The bulk density apparatus was tapped into the measuring cylinder that held a known quantity of blend. The volume occupied by the granule is recorded after about 100 tapings. This indicates the actual volume. Equation was used to determine the true (tapped) density. Weight of powder / true volume equals true density (Pt).

Compressibility index (Carr's Index): -

It has a direct bearing on cohesiveness, particle size, and relative flow rate. This approach to forecasting powder flow characteristics is straightforward, quick, and widely used. A powder's potential strength in a hopper and how easily such an arch could be broken are measured by the compressibility index. [Pt-Pb/Pt] *100 is the compressibility index. Where bulk density = Pb Pt represents actual density

Hausner's ratio

Hausner's ratio is a measure of flow of powder easiness that is not direct. Pt/Pb is the Hausner ratio. In this case, Pt = tapped density Pb is the bulk density. [22]

Herbal Extract Mixture's In-vitro Anti-Obesity

Activity In vitro Inhibitory Activity of Lipase 22

The in vitro inhibitory activity of lipase is a crucial step in evaluating the efficacy of anti-obesity formulations. Lipase, an enzyme responsible for the hydrolysis of dietary fats into free fatty acids and glycerol, plays a significant role in lipid metabolism. The study involves assessing the ability of the polyherbal granules to inhibit pancreatic lipase activity. The assay typically includes incubating the lipase enzyme with a substrate, such as p-nitrophenyl butyrate, in the presence of the herbal formulation. The degree of inhibition is measured by the reduction in the hydrolysis of the substrate, indicated by a decrease in the formation of p-nitrophenol, which can be quantified spectrophotometrically. A significant reduction in lipase activity suggests that the polyherbal granules effectively inhibit fat digestion and absorption, thereby contributing to weight management. This activity is compared against standard lipase inhibitors, such as orlistat, to gauge relative efficacy. The results from the in vitro lipase inhibitory activity provide a preliminary indication of the potential of the polyherbal granules as an anti-obesity agent and guide further in vivo and clinical evaluations.

In vitro α-Amylase Inhibitory Activity 23

Evaluating the in vitro α-amylase inhibitory activity is essential in determining the potential of anti-obesity polyherbal formulations. α-Amylase is an enzyme involved in the breakdown of carbohydrates into simple sugars, which are then absorbed into the bloodstream. Inhibiting this enzyme can reduce the rate of carbohydrate digestion and absorption, thereby assisting in weight management. The assay to measure α-amylase inhibitory activity involves incubating the enzyme with a substrate, such as starch, in the presence of the polyherbal formulation. The amount of reducing sugars released, typically glucose, is measured using colorimetric methods, such as the dinitro salicylic acid (DNS) assay. A decrease in the release of reducing sugars indicates effective inhibition of α-amylase activity by the polyherbal granules. This inhibitory effect is often compared to standard inhibitors like acarbose to evaluate relative potency. The results from these in vitro studies provide valuable insights into the carbohydrate-blocking potential of the polyherbal formulation, suggesting its role in controlling postprandial blood sugar levels and supporting weight management efforts. This preliminary data is crucial for guiding further in vivo and clinical research to confirm the formulation's efficacy and safety in managing obesity.[23]

RESULTS

The oral pharmaceutical dosage form continues to be a widely used method of drug administration despite a number of unresolved issues, such as slow absorption, low acceptance (for example, antibiotics and natural extract-based tablets), bitter taste and even unusual odour, frequent noncompliance issues with younger and older patients, and delayed action. Nonetheless, despite their disagreeable taste, smell, and appearance, natural extracts are very popular as a safe and effective substitute for prescription medications. To address this, the chosen herbal mixture was effectively combined with an advanced pharmaceutical dosage form, such as effervescent granules.

DISCUSSION

Referring to a development in the oral-herbal medicine formulation that offers advantages in quick adsorption, easy usage for most patients since it dissolves quickly in water, and widespread acceptance by all age groups because of its delicious flavour. Six formulae were first created based on the differences in acid-base and flavouring agents. The acids citric acid and tartaric acid were chosen as the acid components based on the appropriate granule properties. In fact, because lemon and peppermint are widely used as flavouring agents and are accepted and popular among Indians, they were chosen to enhance the formulation's taste. In terms of physical examination, batch number six out of the six had the best flow characteristics.

CONCLUSION

Overall, with satisfactory physical qualities, the effervescent granules created from a blend of raw Coffee arabica L. beans, Achyranthes aspera seeds, and Garcinia indica fruit satisfied the Pharmacopoeial quality criteria. A medication may be selectively targeted to one or more enzymes involved in the metabolism of fats and carbohydrates in order to evaluate its anti-obesity impact. The herbal extract mixture was shown to have an inhibitory impact on pancreatic lipase and α amylase, as per the results of in vitro testing. This suggests that the mixture might be useful in treating metabolic problems and aiding in weight reduction. Given their low cost, rapid disintegration, and simplicity in handling and administration, effervescent granules are a viable delivery system for plant nutrients.

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