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Fruitaceutical: A pharmaceutical alternative for fruits

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Abstract
Human beings living all around the globe are moving towards healthy lifestyle which includes: exercise, healthy diet which consists of fresh fruits, vegetables and its related juices, etc. Therefore using medication formulated from natural sources such as fruit powder is gaining popularity due to its conveniences in its use, storage, transportation, and product formulation. The formulation of solid oral dosage form consists of main two parts; firstly, the Active Pharmaceutical Ingredients (APIs) which exhibits the therapeutic effect and secondly, the excipients which works as an additive. This article focuses upon the detail overview about different fruit derived powder use as an excipient in solid oral dosage forms such as tablets, capsules, granules, lozenges, pills, sachets and chewable tablets. Different types of excipients such as diluent, binder, adhesive, disintegrant, lubricant, glidant, coloring agent, flavoring agent, sweetening agent are derived from fruits or fruit parts.

Keywords: fruits, fruit powder, excipients and solid oral dosage form

Introduction
Fruits are grown all over the world for it rejuvenates juice and health benefits. Therapeutic application of bioactive chemicals extracted and purified from fruits, fresh tissues, residual parts and peels have been reported as anticancer, antimicrobial, antiviral, anti-inflammatory apart from nutritional benefits. Utility of these extracts in various industries like food processing, cosmetics and pharmaceutical is due to high amounts of bioactive compounds such as polyphenols, alkaloids, flavonoids, carotenoids, vitamins, tannins, essential oils and minerals.

Increased consumption and production of fruits has led to an increased interest in maintaining their high nutritional levels in addition to a critical prospect toward their aesthetic appearance, it also has a great range scope in pharmaceutical and nutraceutical formulation to cure patient with respect to its disease using appropriate fruit derived essential such as pulp, powder, juice and even its peel. Nevertheless, fruit juice has a high-water water which makes it susceptible to decomposition by microorganisms, chemical and also enzymatic reactions. However, transportation, marketing, stability and storage of fruits are always challenging because of infections and infestations caused by microbial pathogens because of such adverse effect post-reaping preservation and processing of fruit products are necessary. Fruit powder provides several advantages over fruit juices or whole fruit. In terms of preservation and shelf-life fruit powder are helpful in cases related to reduced volume, weight, and packaging requirements, easier preservation, handling, transportation, and storage and increased shelf-life [2-3].

fruit powder is obtained by fruit that has lost almost all of the water content removed through drying methods such as sun drying, solar drying, freeze drying or oven drying. The fruit shrinks during this process, leaving a small energy-dense dried fruit which on further processing converts in into powder form using appropriate conventional methods. Fruit powder are also made from fruit juices using spray drying process which takes place in four basic steps, including atomization, droplet-hot air contact, moisture evaporation and lastly separation of dry product from the air [23]. The main advantages of fruit powder over fresh fruits or their juices are:

1. It can be preserved for much longer period of time than fresh fruit.
2. They consist of very less or no amount of water content. Therefore, contamination via micro-organism or pathogen won't take place.
3. Particularly on long trips where refrigerator is not available fruit powder is a good option.
4. They can be used as a handy snack.
5. Fruit powder contains about the same amount of nutrients as the fresh fruits, but

condensed in a much smaller package.
6. By weight fruit powder contains up to 3.5 times the fiber, vitamins and minerals of fresh fruits.
7. Fruit powders are more stable than fruit juices with respect to shelf-life.

However, fruit powder is dry and granular in nature, it is bulky and highly hygroscopic. Therefore, it is sensitive to the external environment and requires careful handling and packaging during storage, transportation and even during shelf life. Hence, compaction of fruit powder into tablets or any other solid oral dosage form such as tablets, capsules, granules, sachets, lozenges, pills and chewable tablets may be an excellent solution to these challenges. A solid oral dosage form may be more convenient as a health supplement, and this form allows ready storage, transportation, and packaging. Dissolution profile and disintegration time are key factors of fruit powder tablets. However, as the surface area of the powder is reduced when it is placed in tablet form, its hygroscopicity is reduced, and tablets take longer time to dissolve than the powdered form. It can also be prepared into granules which can be reconstituted to liquid form (I.e., sachets).

Fruit powders can be used in pharmaceutical preparation of may solid oral dosage form. It can be used as addition to active ingredients, also known as active pharmaceutical ingredients (APIs). Solid oral dosage form contains a number of inert materials known as additives or excipients. Excipients are now essential parts of the drug delivery system in pharmaceutical dosage form. At a time when synthetic polymers and animal- based products are creating some concerns amongst the users, the need for natural excipients that are safe versatile become more acute.

Excipients present in a formulation must meet certain criteria

1. They must be pharmacologically inert.
2. Cost effective.
3. They must be physically & chemically stable.
4. They must be stable for handling.
5. No interaction with the drug and other components.
6. They must be free from any unacceptable microbiological load.
7. They must be color compatible.

Different kind of fruit powder excipients are

1. Diluents
2. Binder and adhesive
3. Disintegrants
4. Lubricants and glidants
5. Coloring agents
6. Flavoring agents
7. Sweeting agents

1. Diluents

Diluents are fillers used to make required bulk of the tablet when the drug dosage itself is inadequate to produce the bulk.[9] Starch is one of the most traditional excipients used for solid dosage form. Thermally-inhibited starches and powders are used in pharmaceutical products as a diluent, filler, carrier, binder, disintegrant, coating, thickener, moisture sink etc [1]. The starches and powders are inhibited by dehydrating the starch or powder and then heat treating the anhydrous or substantially anhydrous starch or powder for a time and at a temperature sufficient to inhibit the starch or powder.

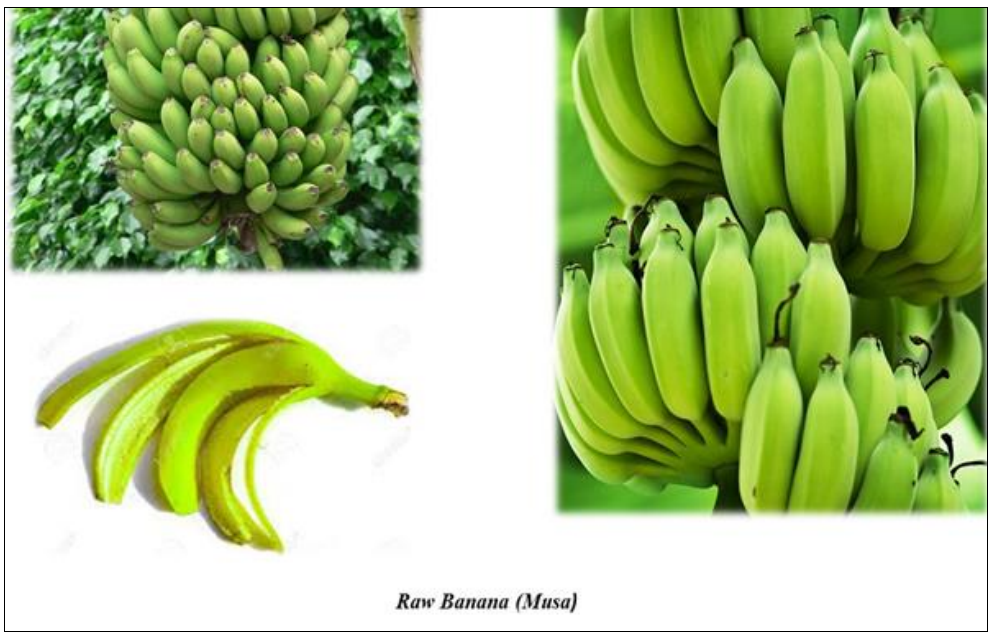

Fig 1: Herbal ingredients as diluent

Raw banana (*Musa*) powder is a very good source of starch and can be used as a pharmaceutical excipient, it can be used as diluent as-well-as binder and glidant. Fully developed raw, green banana are collected and examined visually for any infestation or infection, which compromise the quality of the resulting product. The green banana than peeled to get internal off-white to white part, and cut into pieces ranging in thickness size from 1mm to 3mm followed by drying in a hot air oven at 60°C for 5 hours. This helps in effective drying of pieces, after which they are subjected to grinding until the particle size of powder is sufficiently reduced to the desired size. The green banana powder is strained through sieve no. 125 to get very fine powder ready to be utilized in production of respected dosage form [1].

2. Binder and Adhesive

Tablet binders are one of the most essential elements in the formulation of a tablet. Because they promote cohesiveness, the binders, also called adhesives, help the other ingredients in a tablet to mix together. Binders provides the matrix from which the active pharmaceutical ingredients (APIs) are gradually secreted [2]. Binding agents which have adhesive properties are important excipients, especially for lozenges and tablets. The choice of the particular binder or thickening agent is dependent upon the desired properties of adhesive strength and thickness. These are the dry powders which are added during wet granulation to promote granules or to promote cohesive compact during direct compression. It provides mechanical strength to the tablet [3]. Binders are added to tablet formulation to impart plasticity and thus increase the interparticle bonding strength within the tablet. There are various types of natural binding agent which are formulated from fruits like starch, gums and mucilage are used as binding agent.

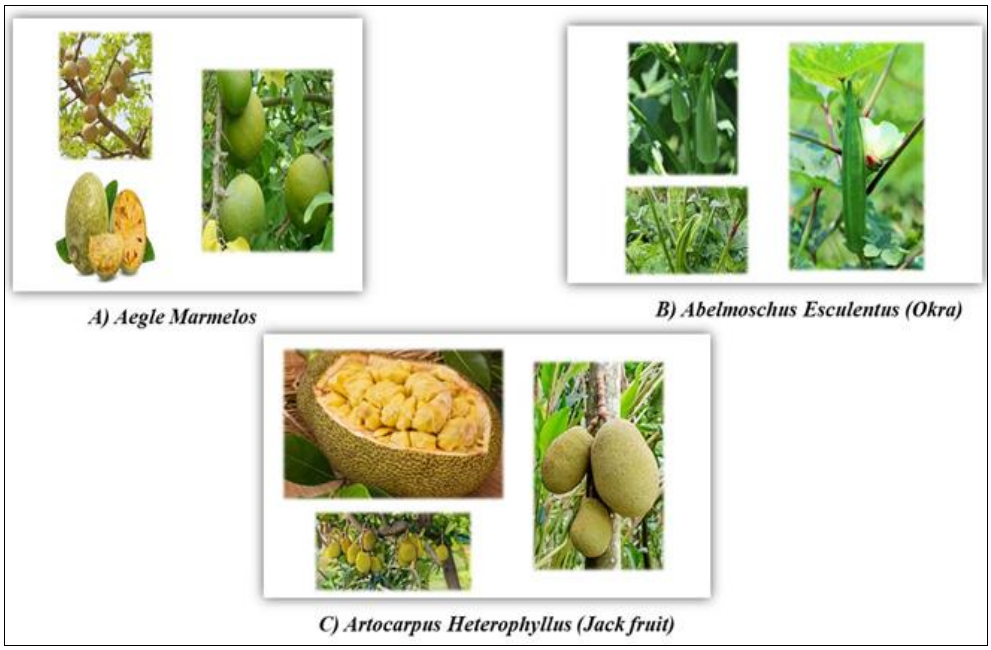

Fig 2: Herbal ingredients as binder and adhesive

Fresh white gum of *Aegle Marmelos* is collected from authenticated plant fruits. The well dried gum is converted to powder form in mortar, and further passed through sieve no. 80 and solubilized in distilled water. The concentrated solution is precipitated in acetone and the resulting precipitate is separated and dried at 600° C [5].

Okra gum (*Abelmoschus esculentus*) is extracted from the pods of Okra fruits. The fruits are cleaned, washed, sliced, crushed and then macerated in distilled water for 10 hours with intermittent stirring. The mucilage is filtered through a white muslin cloth to extract the gum and acetone was added to precipitate the extracted gum. The gum is then filtered under vacuum to remove acetone and dried in desiccators [4].

Mucilage isolated from the ripen pulp of *Artocarpus heterophyllus* (Jack fruit) fruit. The ripe fruit pulp of Artocarpus heterophyllus are separated and seeds were removed. A known amount of pulp is soaked in 2000 ml distilled water for 24 hours, with occasional stirring. The soaked pulp is further ground in the grinder and kept for 24 hours for the release of mucilage, with occasional stirring. After 24 hours, material was squeezed through an eight-fold muslin cloth to separate the marc from filtrate. Further, acetone is added to the filtrate in a particular ratio of 1:3 to precipitate the mucilage. The precipitated fibers are separated via decanting and washed four times with acetone. The mucilage is subjected to preliminary drying in open air for evaporation of acetone and lastly dried in hot air oven at 40°C, powdered and passed through sieve no. 80 and powdered mucilage is obtained [6-7].

3. Disintegrants

Disintegrants are added to oral solid dosage forms to aid in their de-aggregation. Disintegrants are formulated to cause a rapid break-up of solids dosage forms when they come into contact with moisture [9]. Disintegration is typically viewed as the first step in the dissolution process. The objective of a disintegrating agent is to cause the tablet to disintegrate rapidly as to increase the surface area of the tablet fragments and to promote rapid release of the drug. Disintegrants constitute a group of material which comes into the contact with water, swells, hydrate change in volume or form, or react chemically to produce a disruptive change in the tablet.

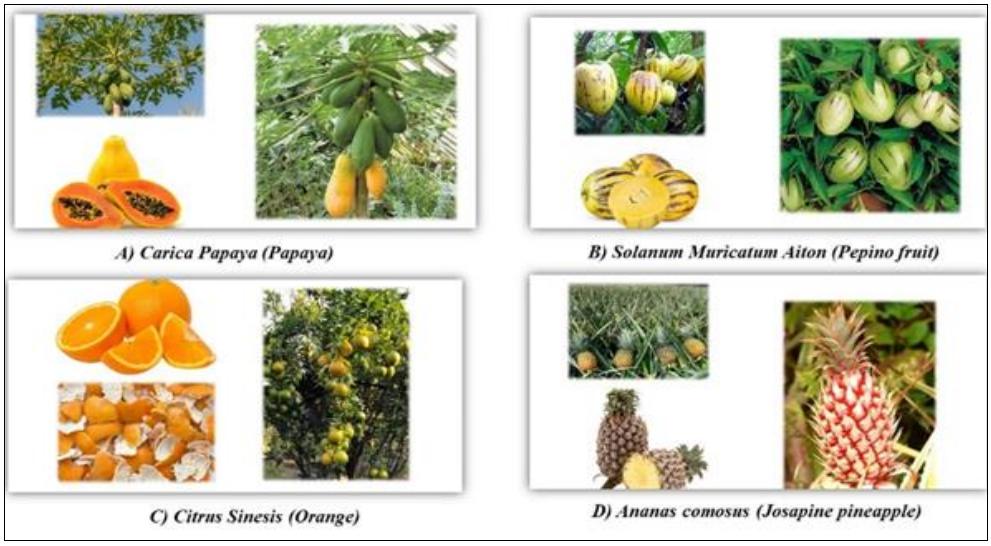

Fig 3: Herbal ingredients as disintegrant

The dried pulp from C*arica papaya* is utilized as tablet disintegrating agent. The papaya pulp powder is obtained from unripe papaya fruit. Firstly, papaya fruit undergoes peeling, removing of seeds, maintaining the essential composition and quality characteristics of natural papaya. The fruits were cut into small pieces, grated, shade dried and powdered. Then it undergoes drying in sunlight first and then in hot air oven. The dried powdered is then milled using a mixer and the resulting powder is allowed to passed through different sieves no. 44, 64 and 80 and made into a fine powder [13-14].

The starch powder isolated by steeping process from pepino fruits (*Solanum Muricatum Aiton*) work as tablet disintegrant. Washed fruits are cut into pieces and steeped in water containing dilute Sulphur dioxide (0.1-0.2%) for more than 2 hours at 48-52°C to break starch from protein bonds and release starch. Softened fruits were then blended with 1% NaCl to free starch from cells. Then milky liquid is filtered through fine muslin with several washes, coarse and fine fibers and part of protein were removed during filtration. On standing, starch granules settle at the bottom and supernatant is then decanted further the wet starch is purified to separate trace amount of protein and soluble materials, by washing with 1% NaCl solution. Finally, settled starch sediment was washed with water and dried at 30-40°C for 30 minutes in a tray drier. Dried product is then collected for further use [15].

Pectin powder extracted from orange peel (*Citrus sinesis*) consist of disintegrating properties. Ripe orange peels are washed carefully and dried under shade for 24 hours, further dried at 30-40° C until constant weight is obtained. Dried fruit peels are then passed through sieve no. 20 and extraction of pectin take place under reflux in a condensed system using water acidified with citric acid to pH 2. Temperature of extraction media is maintained at 70°C and duration of extraction is adjusted about 6 hours. The extractor thimble use for extraction is a Whatman cellulose thimble. Orange peel powder is taken in Soxhlet and process is further repeated to obtain desired amount of pectin [10-11].

Effervescent tablet has been formulate utilizing Josapine pineapple (*Ananas Comosus*) powder having disintegrating property. Fully ripe Pineapple fruits of Josapine variety is used. The crown and skin are removed, then the whole fruit is crushed into pulp using blinder. Now, 20% maltodextrin is added to pulp, this pulp is stored in airtight plastic container and kept in freezer at 20°C for 8 hours. After freezing, the material is transferred to vacuum freeze dryer and dried at 25°C for 48 hours at 0.25m bar and pineapple powder is obtained [16].

4. Lubricants and Glidants

Lubricants is a non-toxic, pharmacologically inactive substance to the formulation to prevent adhesion of the tablet material to the surface of manufacturing equipment such as tablet punches and dies used in the manufacture of solid dosage form [9]. Lubricants are vital excipients for tablets. Whereas glidant (also known as anticaking agents) is also a non-toxic, pharmacologically inactive substance use to promote the flow properties of tablet granulation or powder materials decreasing interparticle friction and cohesion. Natural tablet lubricants exist as either semi solid fats or oils [3].

Starch as lubricants can be used at a concentration of 3-10% w/w during tablets and capsules preparation. Whereas, starch as glidant can reduces interparticulate friction when used at concentration of 2-10% w/w to improve powder and granule flow, especially when using dried starches. Therefore, starch derived from raw banana (*Musa*) and pepino fruit can be used as lubricant and glidant in solid pharmaceutical dosage form formulation such as tablets and capsules [18].

5. Coloring agents

Coloring agents (also called as colorants) are inactive substances which are added into dosage form to produce a distinctive appearance that may serve to differentiate a product from others that have similar physical appearance or even used to protect photo-liable components of the dosage form at some instances.

Anthocyanins are blue, red or purple pigments found in plants especially flowers, fruits, and tubers. The Red, purple and blue colored fruits are commonly consumed for their beneficial effects. The colored pigments of anthocyanin from Berries, Blackcurrants, Jamun and other types of red (I.e., cherries) to blue-colored fruits are strong antioxidants. These colored pigments are potent nutraceutical and pharmaceutical ingredients.

Fig 4: Herbal ingredients as colorants

Ribes Nigrum (Blackcurrant) is well-known for its high concentration of anthocyanins, water-soluble natural pigments. Firstly, frozen Blackcurrants are defrosted in a water bath at 40°C for 30 minutes and grounded using a grinder for 1min 30 seconds to obtain pulp. The enzymes are then added to the grounded material. The use of enzymes is based on their capacity to degrade the cell wall component this leads to increase in the juice yield and also in extraction of bioactive compounds. This juice undergoes spray-drying to dehydrate the juices in order to obtain physically stable powders [20]. *Syzygium Cumini* (jamun) fruits processed into juice. Various additives such as maltodextrin and gum Arabic are used as drying adjunct to facilitate drying process as these carrier agents possess high solubility and low viscosity, an important consideration for spray drying operation. The mixed solution was fed into a pilot-plant spray dryer to get the powder form [19].

6. Flavoring agents

Flavoring agents are added to improve the taste of the product. Either by providing a more pleasant taste or by masking the unpleasant taste. Flavors are vital excipients for chewable tablets, oral disintegrating tablets, dispersed tablets etc. To mask the unpleasant smell as well as taste and make the product more palatable and make it convenient to use by the patient.

Flavoring agents also referred as “masking agents” or “bitter blockers”. Many fruits powder as available in market as flavoring agents. They are mainly concentrated fruit juice dehydrated by spray drying method. Flavoring agent available in the market are: orange (*Citrus aurantium*), raspberry (*Rubus Idaeus*), strawberry (*Fragaria Ananassa*), cherry (*Prunus Avium*) and lemon (*Citrus limon*) flavoring agent.

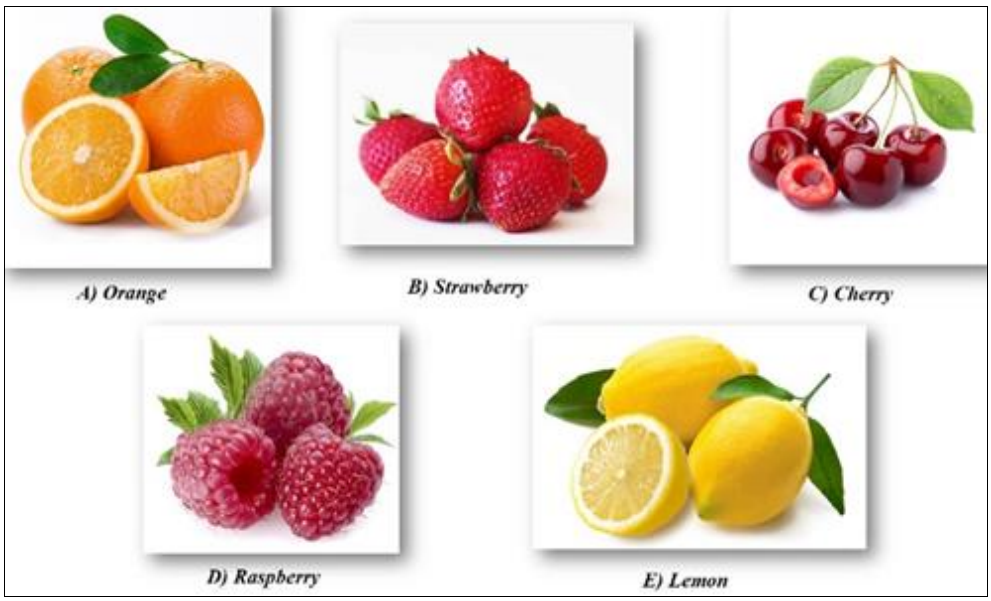

Fig 5: Herbal ingredients as flavoring agents

The production of fruit juice powder is the production of concentrated fruit juices added with drying process. It can be divided into three parts [21, 22]:

1. Raw materials pretreatment: fruit sorting, cleaning, crushing, heating, enzyme treatment.
2. Fruit juice extracting: fruit pulping, juice extraction, clarification (for making clear juice), homogenization and degassing (to make cloudy juice).
3. Juice processing: fruit juice concentration, drying (spray drying), cooling, packing.

7. Sweetening agents

Sweetening agents are also called as sweeteners. Sweeteners are the substance to mask the unpleasant taste and sweeten the oral dosage forms. It also masks the unpleasant flavors. It works by binding to the receptors present on the tongue that are responsible for the sensation of sweetness. Sweeteners are vital excipients for chewable tablets, lozenges, oral disintegrating table, oral solution, emulsions and oral suspension.

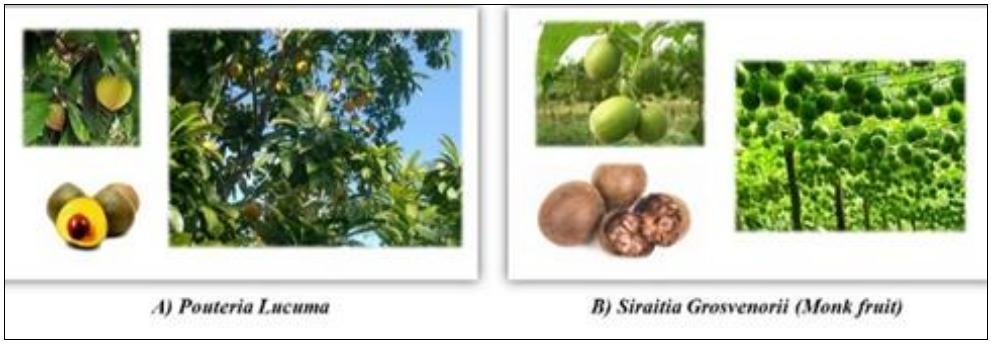

Fig 6: Herbal ingredients as sweetening agents

Lucuma powder is a low-sugar natural sweetener made of dried, ground lucuma (*Pouteria ucuma*), a fruit that grows on lucuma trees found mainly in Andean valleys of Bolivia, Chile, Ecuador, and Peru. Lucuma powder consist of sweet taste and health benefits. It has become a popular natural substitute for refined sugar and artificial sweeteners. Powder form of lucuma tastes like butterscotch. Lucuma consist of rich source of nutrients including beta-carotene, vitamin B3, iron, zinc, calcium, magnesium and other vitamins and minerals. It also has antioxidant, anticancer and Anti-inflammatory properties [25].

Monk fruit sweeteners extracted from monk fruit (*Siraitia Grosvenorii*) a small, round fruit grown in southeast Asia. The Monk fruit is known as Buddha fruit. Monk fruit sweeteners is a natural, zero-calorie sweeteners. It is high in unique antioxidants called Mogrosides, which make it 100-250 times sweeter than regular sugar. It consists of different properties such as anti-diabetes, anti-cancer properties, anti-inflammatory and antioxidant. It's formed by removing the seeds and skin of fruits and crushing it to collect the juice, which is then dried into a concentrated powder. Monk fruit contains natural sugars, mainly fructose and glucose [24].

Conclusion

The use of natural products for improving human health has evolved independently in different regions of the world, gaining wide acceptance in both developing and advanced countries and are being produced in commercial quantities. Therefore, a more consistent approach to the evaluation of nutrient-drug interactions in human beings is needed in suitable dosage form using fruit powder which are rich in minerals, vitamins, phytochemical and also enzymes that simply suits the current trends of a healthy lifestyle [17]. Spray drying is an economical method for producing dry powders. It is a useful method for increasing shelf-life and stability of colorant which helps in easy handling by reducing volume. Normally the fruit powder is very dry, hygroscopic in nature and bulky in volume. So, during storage, transportation and handling it requires special. To overcome these problems compaction of fruit powder derived from raw bananas, Pepino fruits, Aegle marmelos, Abelmoschus Esculentus, Jack fruit, Papaya, Orange, Pineapple, Raspberry, Jamun, Cherry, Lemon, Strawberry, Blackcurrant, Lucuma fruit and Monk fruit can be utilize as an excipient for the tablet formulation is a unique technique. This helps to reduce the volume as well as the surface area, which also reduces hygroscopicity of the powder and also exhibits good quality control. The stability of these fruit powder containing products is of paramount importance to assure product quality, safety and efficacy [2]. It is expected that fruit powder product manufacturers will apply the necessary protocols and techniques to achieve and maintain the stability of their products during manufacture, storage, transportation and usage. This will contribute to patient safety, product efficacy and enhance patient confidence in fruit powder products and improve compliance.

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