

REVIEW OF CISSUS QUADRANGULARIS- BASED HERBAL TABLETS: A NATURAL APPROACH TO OSTEOPOROSIS MANAGEMENT

*Ketaki Sanjay Phalke and Hemant Suresh Kandle

Rajarambapu College of Pharmacy, Kasegaon.

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*Corresponding Author: Ketaki Sanjay Phalke
Rajarambapu College of Pharmacy, Kasegaon.

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ABSTRACT

Herbal effervescent tablets are a novel dose form that combines the benefits of herbal medication with the convenience of effervescent technology. This review article gives an outline of the formulation, pharmacological activities, and therapeutic applications of herbal effervescent tablets. The article talks about the different herbal extricates that can be used in effervescent tablets, including *Cissus quadrangularis*, and their potential wellbeing benefits. The formulation perspectives of herbal effervescent tablets, including the utilize of effervescent agents, excipients, & fabricating innovations, are too reviewed. The article highlights the potential helpful applications of herbal effervescent tablets, counting the treatment of osteoporosis, obesity, and diabetes etc.

KEYWORDS: Herbal effervescent tablets, *Cissus quadrangularis*, formulation, pharmacological activities, therapeutic applications.

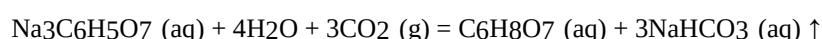
1. INTRODUCTION

The oral dose forms are the foremost common route of medicate administration in spite of having a few drawbacks like moderate retention, and in this way the onset of activity is drawn out. This can be surpass with delivering the medication through fluid form; however, many APIs have limited the durability in the state of liquid. So, effervescent tablets serve the purpose of an optional method of administration. Effervescent tablets offer an innovative method to through oral tradition drug administration, providing rapid discharge the compounds that are active and increased bioavailability, improved patient compliance. As an outcome, effervescent tablets provide an alternative to conventional tablets.^[1,2]

1.1 Definition

According to USFDA, effervescent tablets are aiming to broken down or dissolved in liquid some time recently administration. Effervescent tablets discharge CO₂ produced. when an acidic substance interacts with sodium bicarbonate in favor of liquid. The most prevalent acids used are citric acid, tartaric acid, and, adipic acid, fumaric acid. Bicarbonates utilized are potassium bicarbonate and sodium bicarbonate. In these tablets, starch, cellulose, polyvinylpyrrolidone, gelatine, povidone, hydroxypropyl cellulose and hydroxypropyl methyl cellulose is utilized as binder.^[3,4]

Effervescent tablets have extraordinary property which permits faster absorption of the medicate. Effervescent tablets are outlined in the process that crumbles Whenever they come in interaction with fluids such as waters or juice, especially the medication breaks down into a substance that dissolves.



Water + Carbon dioxide + Sodium citrate + Citric acid = Sodium bicarbonate + Sodium citrate despite just a single drop of solvent may activate this response, alongside because fluids represents one of the resultant goods its presence increases the Efficacy of the method causing it difficult to cease it. As a result, minimal water connection is incorporated towards all aspects of fabrication and capacity of bubbling products.^[5,6]

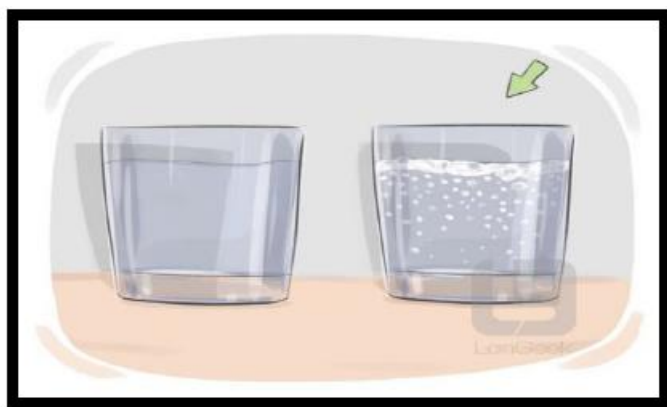


Fig. 1: Effervescent tablet reaction.

1.2 Advantages^[7,11]

Here are a few benefits of effervescent tablets

1. Fast Disintegration: Effervescent tablets break up rapidly in water, discharging the active ingredients quickly, which can lead to faster onset of activity.
2. Progressed Bioavailability: The quick disintegration of effervescent tablets can improve the bioavailability of the main ingredients, making them more viable.
3. Convenient: Effervescent tablets are simple to administer, as they can be essentially dipped in a container of water. making them perfect for patients who have trouble swallowing tablets or capsules.
4. Stable: Effervescent tablets can be more steady than liquid formulations, as they are less prone to degradation and oxidation.
5. Patient Compliance: The Effervescent tablets can progress quiet compliance, as they are simple to manage and can

be taken on-the-go.

6. Targeted Delivery: Tablets can be outlined to discharge the active ingredients in a particular area, such as the stomach or guts, which can progress their adequacy.

1.3 Disadvantages^[7,11]

Here are a few prons of effervescent tablets

1. Limited Stability: Effervescent tablets are delicate to moisture and stickiness, which can cause them to debase or lose their strength.
2. Short Shelf Life: Effervescent tablets ordinarily Have a shorter lifespan. than other dosage forms, as they are more inclined to debasement and oxidation.
3. Difficulty in Formulation: These tablets can be challenging to formulate, as the active ingredients must be consistent with the effervescent agents and the tablet must be outlined to discharge the active ingredients quickly.
4. Taste and Odor Issues: Effervescent tablets can have obnoxious tastes and odors, which can influence patient compliance.
5. Gastrointestinal Irritation: Effervescent tablets can cause gastrointestinal disturbance, such as acid reflux, corrosive reflux, and stomach disturbed, especially in case taken on an purge stomach.
6. Quality Control Issues: Tablets can be challenging to fabricate and quality control, as the effervescent response can be influenced by different components, such as temperature, stickiness, and tablet composition.

2. CISSUS QUADRANGULARIS

Cissus quadrangularis may be a year-round grape plant. It is commonly referred to as Veldt Grape or Devil's Backbone. With regard to the capability to connect cartilage., a herb is referred to as "bone setter" (Hodjod in Hindi & Asthisandhani in Sanskrit). *Cissus quadrangularis* is used for its therapeutic plant. In Siddha pharmaceuticals, it is regarded as a refreshing and pain reliever. It is also used for the repair of cracked bones, harmed tendons, and cartilage, thus its name asthisamharaka (which typically which prevents bone deterioration). The new stem and takes off of CQ are utilized for the treatment of menstrual disorder, haemorrhoids, scurvy and flatulence.^[12,13]



Figure 2: *Cissus quadrangularis* plant.

2.1 Taxonomic Classification.^[14]

- Kingdom : Plantae – Plants
- Subkingdom : Tracheobionta – Vascular plants
- Superdivision : Spermatophyta – Seed plants
- Division : Magnoliophyta – Flowering plants
- Class : Magnoliopsida – Dicotyledons
- Subclass : Rosidae
- Order : Rhamnales
- Family : Vitaceae – Grape family
- Genus : Cissus L. – treebine P
- Species : Cissus quadrangularis L. – veldt-grape

2.2 Chemical Constituents

Phytochemical experiments on methanol extract revealed an abundance of triterpenes. counting α - and β - amyrins, β -sitosterol, ketosteroids, phenols, tannins, carotene and vitamin C. Seven alicyclic lipids constituents have moreover been detailed from *Cissus quadrangularis*. A few unsymmetric tetracyclic triterpenoids such as 21b-diol, d- amyrone, d- amyrin, onocer-7-ene-3a, and 3,3',4,4'-tetrahydroxybiphenyl has been isolated from this plant. A few additional components, which include quercetin, stilbene and flavonoids, kaempferol, subsidiaries, quadrangularins A, B, and C, and numerous more, such as, perthenocissi, pallidol, phytosterols , resveratrol, and piceatanon, , have been isolated from the plant. Stem extricate consists of a high concentration of calcium particles and phosphorus, which are both essential for the development of bones.^[15,16,17]

2.3 Pharmacological Profile

The plant's primary traditional use is to heal fractures and produce antifungal, anthelmintic antibacterial and, anti-haemorrhoidal, antioxidant and pain-relieving properties. The production of cancer-prevention agents in the free radical push and lipid digestion systems, gastroprotective activity, and NSAIDs belong to the additional potential health care effects. Because of its numerous beneficial properties and expanded applications, the plant has the potential to be an important therapeutic herb.^[18,19]

Table 1: Pharmacological profile of *Cissus quadrangularis*.

Sr. no	Pharmacological activity	Mechanism of action	Therapeutic application
1	Anti inflammatory	Inhibits COX-2 & iNOS	Osteoarthritis, rheumatoid arthritis
2	Antioxidant	Scavenges free radicals	Neurodegenerative disease, cancer
3	Anti – diabetic	Stimulates insulin secretion	Type 2 diabetes
4	Anti- obesity	Inhibit lipogenesis	Obesity
5	Bone health	Stimulate osteoblast activity	Osteoporosis
6	Cardiovascular health	Lower blood pressure	Hypertension
7	Neuroprotective	Protects against neurodegeneration	Alzheimer's disease, Parkinson's disease

3. OSTEOPOROSIS

Osteoporosis is the result of an imbalance within the bone remodeling handle in which the degree of bone resorption exceeds the rate of bone arrangement, and thus, the bone mineral thickness declines. This phenomenon expanded the chances of fracture. Osteoporosis may be an unnoticed worldwide disease. It has become a serious health risk in recent

decades, influencing more than 2000 million people worldwide. This is a long-term, dynamic scenario characterized by micro-architectural weakening of tissue in the bone that occurs with low bone density. Osteoporosis fractures most commonly occur in the wrist, spine, shoulder, and hip. Osteoporosis accounts for more than 80% of all breaks in people across the age limit of fifty. Every year, osteoporosis causes 70-90% of the 30,000 hip breaks that occur. Twenty-eight percent of women and 37% of men who have a hip break will pass away within a year.^[20,22]

3.1 Etiology of Osteoporosis

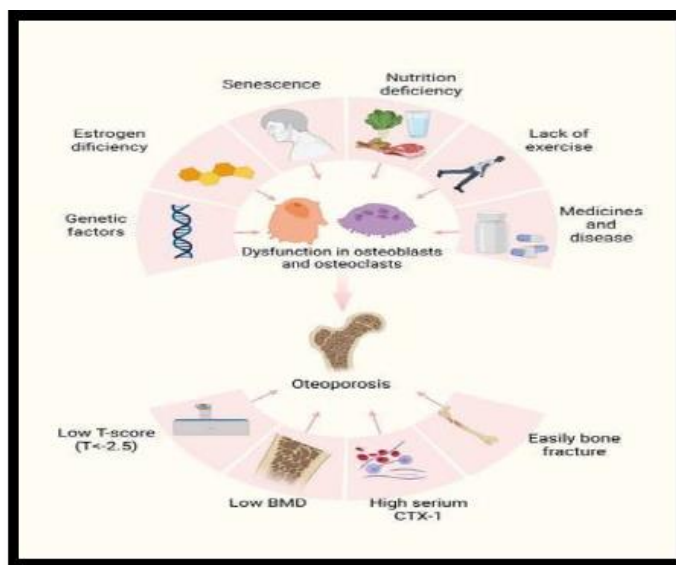


Fig. 3: Etiology of Osteoporosis.

In spite the fact that several risk variables have been identified as increasing the likelihood of developing this illness, such as Caucasian race, advanced age, female sexual orientation, previous instances of cracking, nicotine, and alcohol abuse, the exact reason of osteoporosis has yet to be determined. Some theories about the origins of osteoarthritis include cartilage cell senility, lifestyle factors (primarily exercise and nutrition), and deterioration of the vitamin D digestion system with age. The last-mentioned hypothesis implies that aging causes an inadequate absorption of vitamin D. Activated vitamin D may be an indicating atom involved in the regulation of intestinal calcium absorption. As a result, a poor vitamin D digestion system reduces absorbs calcium in the intestine, prompting the endocrine system to eliminate calcium from the bones. Eventually, such persistent calcium loss from the bones leads to decreased bone mass & advancement of osteoporosis.^[23]

3.2 Treatment

There are a variety of medicines employed to manage osteoporosis., including antiresorptive drugs that slow bone loss, cartilage developing medication that help shape the skeleton, and more complex medications. In addition to medication treatment, calcium supplementation & vitamin D may be directed to make sure adequate intake and maximum efficacy of medicinal treatment. Bisphosphonates prevent osteoclast. They serve as the primary treatment option for several kinds of bone digestion system diseases which involve extensive resorption of bones. SERMS resemble female hormones in some tissues and anti-estrogens with other individuals, providing the bone-retention benefits of estrogen lacking the negative adverse effects. Presently, the solely promoted SERM is raloxifene. Raloxifene anticipates bone misfortune and it is empirically proven to prevent and treat fractures of vertebrae in postmenopausal women.^[23]

4. CISSUS QUADRANGULARIS AND OSTEOPOROSIS

Cissus quadrangularis acts as an inborn beneficial plant from the Indian nation. This plant is used by society to advance the fracture-healing process since ancient times. Chakra Dutta and Bhava Prakash recommended it in old Ayurvedic writings as a common tonic, particularly for ruptured patients.

Cissus quadrangularis includes large quantities of vitamin C, carotene A, anabolic steroids, and calcium. All of these anabolic steroidal standards from *Cissus quadrangularis* appeared to have a controlled affect on the process of break restoration via affecting the fast recovery for every connective tissue of mesenchymal source, specifically fibroblasts, chondroblasts, and osteoblasts involved in the recovery and faster formation of minerals in the callus. It also has a stronger effect on new bone cell expansion compared to additional reactions within cells.^[23]

COMMERCIAL PRODUCTS OF CISSUS QUADRANGULARIS

- Flexi- muv oil (Anti-inflammatory, Anti – arthritic)
- Boneforte capsules (Calcium supplements)
- Laksha gogglu (Analgesic, Anti-inflammatory)
- Bixa botanicals Powder
- Zespo *Cissus quadrangularis* 1000 mg Capsule
- Merlion naturals Hadjod Tablets

5. FORMULATION AND ASSESSMENT OF HERBAL EFFERVESCENT TABLET

5.1 Fundamentals of Effervescent^[24,25]

Effervescence is composed of a dissolvable natural acidic substance and a soluble base metal carbonate salt, among these is typically the API. Carbon dioxide is produced when this blend involves towards interaction with liquid. Typical illustrations regarding the alkaline and acidic substances used include:

Table 2: Component of effervescent tablet Alternative Components.

Dissoluble acids with organic omponents	Alkaline metal carbonate salt.
• Citric acid • Tartaric acid • Malic acid • Fumaric acid • Adipic acid	• Sodium bicarbonate • Sodium carbonate • Sodium sequicarbonate • Potassium carbonate • Potassium bicarbonate

Table 3: Alternative component of effervescent tablet.

Acids	Alkali metal carbonate salt
Glycolic acid	Calcium carbonate
Lactic acid	Magnesium carbonate
Succinic acid	Zinc carbonate

5.2 Formulation Methodologies

1. WET GRANULATION^[26]

Wet granulation is the foremost commonly used agglomeration strategy within the pharmaceutical industry. The method of wet granulation essentially includes damp massing with a granulating dissolvable, damp scaling and drying of the powder blend process of wet granulation are as follows:

- Blending of the drug(s) and excipients.

- Preparation of binder solution.
- Blending of solution of binder with mixture powder to make damp mass.
- Drying of damp granules.
- Blending of granules with lubricant, disintegrant, glidant.

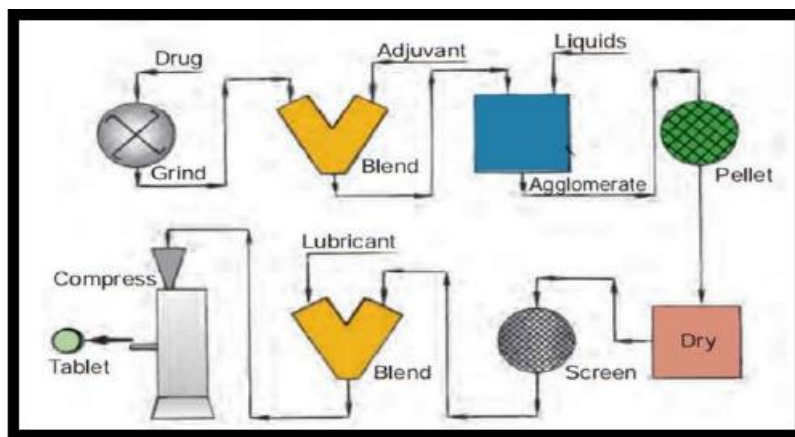


Fig. 4: Wet granulation diagrammatic representation.

2. DRY GRANULATION ^[27,28]

Dry granulation is the least desirable method of granulation method. This process involves blending the powder is squeezed without any warm and dissolvable. It involves two strategies are utilized.

1. Slugging it is most used. This strategy involves recompressing the particles and processing the resulting tablets or slugs to remove granules.
2. Another strategy is to recompress the fine powder with compelled rolls using an instrument like a Chilsonator.

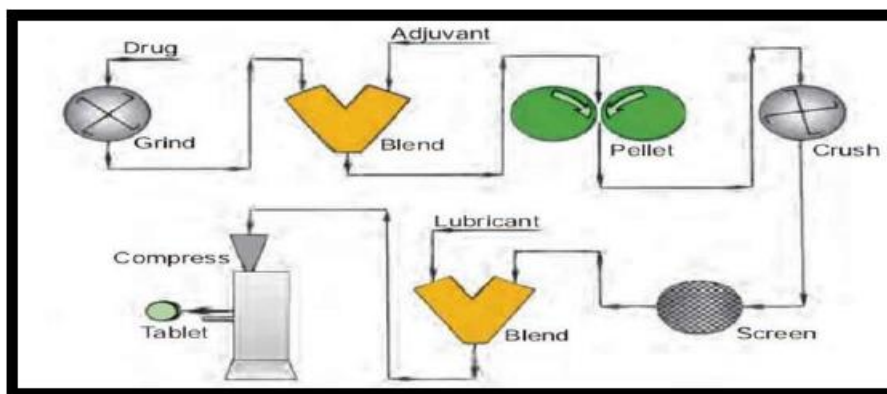


Fig. 5: Dry granulation diagrammatic representation.

3. DIRECT COMPRESSION ^[29,30]

It is the process of pressing the finely ground product into the tablets. Direct compression is used when the drug accounts for a significant amount of the tablet's entire weight. Tablets including 25% or less of medicate compounds can be made with an appropriate diluting agent that serves as a the provider or vehicle for the drug. Tablets are formed and compacted using an instrument that may have one or more terminals.

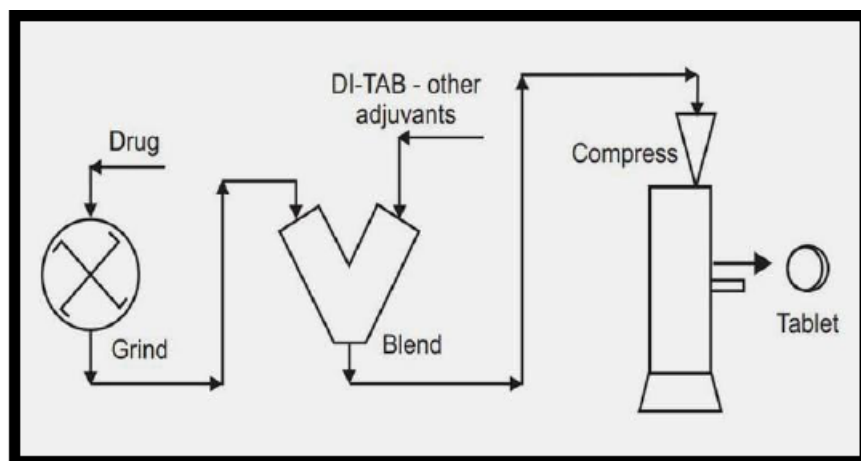


Fig. 6: Direct compression diagrammatic representation.

5.3 Pre Compression Evaluation

1. Bulk Density^[32,33]

It is a measurement of the overall mass to B.V of powder. The starting amount was measured after adding 25 g of granules to a 100 ml measuring cylinder. This introductory amount is known as the bulk volume. using it, the B.D is calculated by formula given as follows. It is communicated in gm/ml and provided via

$$\text{Bulk density} = \frac{\text{Weight of specimen}}{\text{Amount occupied by the sample}}$$

2. Tapped Density^[31,33]

It represents the proportion of the powder's total mass to its tapped volume. The volume was measured by tapping the measuring cylinder in increments of 10, 50, and 100 times. It is communicated in grams per milliliter.

$$\text{T.D} = \frac{\text{Weight of the Sample}}{\text{Tapped amount}}$$

3. Hausner's ratio^[36,37,38]

It is used to predict powder characteristics for flow and is determined as the ratio of density of the tapped to bulk mass.

$$\text{Hausner's ratio} = \frac{\text{T.D}}{\text{Bulk Density}}$$

4. Compressibility index^[36,37,38]

The compressibility index is an imperative measure which is calculated from both the bulk and tapping density values. The compressibility index demonstrates powder flow characteristics. It is communicated as percent and given by,

$$\text{Compressibility index} = \frac{\text{TD} - \text{BD}}{\text{Tapped density}} \times 100$$

Table 4: Hausner's ratio & compressibility index

Sr. No	Flow Character	Hausner's ratio	% comp. index
1	Excellent	1.00 - 1.11	< 10
2	Good	1.12 - 1.18	11-15
3	Fair	1.19 - 1.25	16-20
4	Passable	1.26 - 1.34	21-25
5	Poor	1.35 - 1.45	26-31
6	Very poor	1.46 - 1.59	32-37

5. Angle of Repose^[31,34]

It is used to define the flow properties. The angle of repose indicates the possibility of a friction force between particles. It is the most extreme angle that can be formed by the granule heap's surface and the plane of the horizontal.

$$\Theta = \tan^{-1} h/r$$

Table 5: Angle of repose

Sr. no	Angle of repose	Powder flow
1	25-30	Excellent
2	31-35	Good
3	36-40	Fair
4	41-45	Passable
5	46-55	Poor
6	56-65	Very poor
7	>66	Extremely poor

7.6.2 Post compression parameters**1. Hardness Test**^[39]

Tablets' aversion to transportation or destruction within the circumstances of capacity, shipping, and care prior to use is determined by their hardness. The hardness of every formulation's tablet had been determined using a Monsanto Hardness Analyzer. The hardness was expressed in kilograms per square centimetre. The ideal hardness ranges from 4 to 10 kg/cm².

2. Tablet Thickness Measurement^[40,41]

Calibrated vernier calipers were utilize for thickness measurement of the tablets for every composition. The mean thickness varieties should not deviate by more than 5% from their limits.

3. Friability Test^[40,42]

friability of the tablet was determined using the Roche friabilator. Take 20 tablets from each formulation, weigh them, and then place them in a friabilator for 4 minutes at a speed of 25 rpm, for a total of 100 revolutions. Tablets were cleaned with a fine muslin cloth and again weighed. The USP limit is 0.5-1%. The formula determines the friability (F).

$$\text{Friability (\%)} = \frac{\text{Beginning weight (W1)} - \text{The last weight (W2)} \times 100}{\text{Last weight (W2)}}$$

4 Weight variation^[40,43]

The weighed twenty of the tablets separately, estimated the mean weight, and contrasted each of the tablet weights to the normal. Complies the tablet test if not greater than two above the number of percent specification & none of them varies by a percentage greater than the limitation.

Table 6: Weight variation.

IP/BP	Limit	USP
Less or 80 mg	10 %	Less or 130 mg
80 mg or more or 250mg or less	7.5 %	130 mg to 324 mg
More than 250 mg	5 %	More than 324 mg

5. Assessment of effervescence time^[44]

The one tablet is placed in a container containing 200 ml of decontaminated water at $20^{\circ}\text{C} \pm 10^{\circ}\text{C}$. Once a clear solution without particles is obtained, the effervescence time is complete. The average of three estimations for each formulation is to be reported.

6. Disintegration time^[1]

The process of breakdown of a tablet into smaller particles is called as disintegration. Six tablets, one at a time are tested in a beaker containing 200 ml of water at 15°C - 25°C . when the evolution of gas ceases, the tablet has disintegrated, being either dissolved or dispersed in water so that no agglomerates of particles remain. A 5 min time limit is specified.

7. Identifying the effervescent solution pH^[45]

To determine the pH of the solution, dissolve a single tab in 200 ml of decontaminated water at $20 \pm 10^{\circ}\text{C}$ and use a pH meter upon passing the breakdown duration. Perform the test three times for each of the preparation.

8. CO₂ Content Measurement^[43]

A single effervescent tablet was dissolved in hundred ml of 1 N sulfuric acid solution, and variation in weight were determined at the end of the dissolution process. The resulting variance in weight corresponds to the quantity (mg) of CO₂ for every tablet. Studies a mean of three assessments.

9. % Drug Content^[41]

Drug content estimation is the systematic measurement and analysis of the amount of active pharmaceutical ingredients in various formulations to ensure proper dosage and effectiveness. This process involves techniques like UV spectrophotometry, which allows for accurate determination of drug concentration in tablets. By preparing stock solutions and measuring absorbance, the method ensures uniformity and compliance with specified dosage.

$$\% \text{ Drug content} = \frac{\text{Absorbance of sample} \times 100}{\text{Absorbance of standard}}$$

10. Stability Studies^[40,49]

The ability of a particular formulation in a particular container to stay within its beneficial, toxicological, chemical, and physical parameters is known as stability of a drug.

The goal of Testing for stability provides proof that shows how the potency of a medicinal substance or drug item changes periodically due to a number of external variables involving temperatures, stickiness, and light, allowing suggested capacity conditions, re- test period, and shelf lives to be determined.

ICH indicates the length of the study and the capacity conditions.

Long-term testing at $25 \pm 2^{\circ}\text{C}$ and $60\% \pm 5\%$ RH for 12 months

Accelerated testing at $40 \pm 2^{\circ}\text{C}/75\% \pm 5\%$ RH for 6 months.

Stability tests for a few chosen formulations were carried out in this study for a maximum of three months at $40\pm 20^{\circ}\text{C}$ and $75\pm 5\%$ relative humidity.

CONCLUSION

Effervescence is defined as the formation of gas bubbles from a fluid because of a chemical reaction. The foaming tablets provide several benefits, including faster release of the api, increased bioavailability, and improved patient compliance. The development of herbal effervescent tablets containing *Cissus quadrangularis* is a promising approach for the treatment of a variety of health issues. Utilization of employment of effv. Agents can help to improve the solvency and steadiness of *Cissus quadrangularis*. The audit concluded that *Cissus quadrangularis* extract has important pharmacological activities such as anti-inflammatory, antioxidant, and anti-diabetic properties.

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