



**3RD HEALTH SCIENCE  
INTERNATIONAL CONFERENCE**

## The 3rd Health Science International Conference (HSIC)

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This collection contains selected papers from the **3<sup>rd</sup> Health Science International Conference** held in Malang, Indonesia on 5<sup>th</sup> October 2022. This event was hosted by the Faculty of Health Science University of Muhammadiyah Malang, Indonesia.

The conference was held to bring together leading scholars and practitioners in medicine with the goal of reflecting on holistic patient care and support.

This *KnE Medicine* collection contains 40 peer-review papers that deal with the medical ailments of the everyday person. Researchers in this issue advocate for integration between Western and Eastern medicine to deliver cohesive treatment plans for people suffering from a wide range of issues. While Western medicine can provide immediate medical attention to life-threatening cases, Eastern medicine successfully develops sustainable treatment plans that aim to support the natural healing capabilities of the human body. Therefore, this collection aims to offer a balanced approach to patient care that blends practices from both medical traditions, providing holistic remedies for muscle pain, pregnancy, sleep disorders, and more.

These papers will be of interest to academics, students, or professionals researching or working on healthcare innovation, patient care, holistic medicine, and nursing.

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**HSIC**  
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Conference Chairman

## Research Article

# Effervescent Tablets Formulation of Jicama (Pachyrhizus erosus) Extract with Various Concentrations of Binders and Sweeteners

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**ORCID**Dyah Rahmasari: <https://orcid.org/0000-0002-0727-4392>**Abstract.**

Osteoporosis is a major public health problem. Exogenous estrogen or Hormone Replacement Therapy (HRT) is the potential therapy for osteoporosis. Still, the patient rarely chooses this treatment because of the risk of breast and endometrial cancer. Phytoestrogens or estrogen-like compounds, particularly isoflavones, are a potentially safe alternative to HRT. Jicama (*Pachyrhizus erosus*) is a plant that contains many phytoestrogens. This research aimed to determine the physicochemical characteristics of jicama extract in effervescent tablets with various concentrations of binder and sweetener. The manufacturing of jicama effervescent tablets used raw materials extracted from 96% p.a. ethanol by maceration. The extract is then formulated with various binder concentrations (PVP 40 and gelatin) and sweeteners (lactose and Mannitol) using the wet granulation method. Based on the test results on the physicochemical properties of tablets, all the formula meets the requirement of a good tablet, and the preferred formula is Formula 4 with 0.75% of PVP40 and 47,75% Mannitol. Ethanol extract of jicama can be formulated into effervescent tablets and has the potential to be developed as a treatment for osteoporosis.

**Keywords:** Xicama Extract, Fitoestrogen, Estrogen-like therapy, Osteoporosis, Effervescent tablet

## 1. INTRODUCTION

There is a decrease in estrogen secretion by the ovaries, as women get older, causing bone fragility or commonly called osteoporosis (1). This results in an imbalance between bone resorption and bone formation, thereby accelerating the loss of bone mass and structural decay of the skeleton (2). Osteoporosis is a health problem that is widely recognized as a world health problem. In the USA, this disease affects 8 million women and 2 million men, of which 55% are people aged 50 years or more (3). Treatment of osteoporosis is done by administering anti-resorptive agents such as risedronate and alendronate. Then you can also use thiazide diuretics, calcium, vitamin D, calcitonin, or Selective Estrogen Receptor Modulators (SERMs) such as raloxifene (4). In addition to

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these drugs, exogenous estrogen or Hormone Replacement Therapy (HRT) has been developed as a treatment for osteoporosis which can reduce the reduction in bone mass and reduce the risk of fracture. However, this treatment is rarely chosen by patients because of unwanted side effects and the risk of breast cancer and endometrial cancer (5). So, there is a need for non-hormonal therapy or therapy from natural ingredients that can be accepted as a treatment for preventing osteoporosis.

Phytoestrogens or estrogen-like compounds, especially isoflavones, are potential safe alternatives for Hormone Replacement Therapy (HRT). Phytoestrogens are produced by plants and have the same function as endogenous estrogens (6). Isoflavones are secondary metabolites found in various plant parts such as fruits, vegetables, grains, flowers, roots, barks and stems, which has the potential to maintain and improve the bone mass of human subjects and develop into antiosteoporotic drugs (7). Isoflavones stimulate osteoblastic bone formation and prevent osteoclastic bone resorption based on genomic and non-genome effects involving estrogen receptors so as to increase bone mass (7–9). *Pachyrhizus erosus* or Jicama is a plant that contains phytoestrogens. Jicama contains phytoestrogens, namely daidzein, daidzin, genistin, daidzein-7-O- $\beta$ -glucopyranose, (8,9)-furan-yl-pterocarpan-3-ol, 5-hydroxy-daidzein-7-O- $\beta$ -glucopyranose, 4-(2-(furan-2-yl)ethyl)-2-methyl-2,5-dihydro-furane-3-carbaldehyde, and 2-butoxy-2,5-bis(hydroxymethyl)-tetrahydrofuran-3,4-diol (10,11).

Effervescent tablets are uncoated tablets generally containing carbonates or hydrogen carbonates and acid substances, which react rapidly in the presence of water to release carbon dioxide (CO<sub>2</sub>) gas simultaneously. Effervescence is defined as the evolution of gas bubbles from a liquid mixture as a result of a chemical reaction and meant to mask undesirable taste of medicinal agents (12). Usually, these tablets are prepared by compressing the active ingredients with mixture of sodium bicarbonate and organic acids such as citric and tartaric acid. This tablets can be prescribed to patients who suffered from swallow capsules or tablets. The main advantages of effervescent tablets are quick production of solution, which is faster and better to absorb (13).

Therefore, researchers are interested in conducting research on the use of isoflavone phytoestrogens in jicama and processing them into products that are easier to consume, namely effervescent tablets as a treatment for osteoporosis. This product is produced and controlled same as conventional tablets. These controls are included granule evaluation (Hausner's ratio, angle of repose, compressibility index, moisture content, and particle size determination) and tablet evaluation (weight variation, thickness, hardness test, friability test, pH value, and effervescence time).

## 2. MATERIALS AND METHODS

### 2.1. Instruments

Analytical balance, single-punch press machine, friability tester, sieve shaker, oven, moisture balance, hardness tester, pH meter, miller and vernier calipers.

### 2.2. Ingredients

Jicama (*Pachyrhizus erosus*) tuber extract were obtained from Materia Medika Batu, Indonesia. Ethanol 96% was purchased from Sigma Aldrich in pro analysis grade. Lactose, mannitol, citric acid, tartaric acid, sodium bicarbonate, saccharin, gelatin, PVP 40, Mg stearate, and orange flavouring agent in technical grade.

### 2.3. Effervescent Tablets Formulation of Jicama Extract

The formulation of an effervescent tablets of jicama extract was made according to the formula presented in Table 1. Firstly, materials of each formulation were weighed for preparing the granules. Citric acid, tartaric acid, sodium bicarbonate, and were milled by using miller and were blended for 10 minutes. Then PVP 40 / gelatin solution in 96% ethanol and orange flavouring agent was added with the mixture and continue by entering lactose/mannitol as a diluent. This wet mass was passed through sieve No. 12 and the granules were dried in an oven at 50°C for 30 minutes. Then, the dried mass was passed through sieve No. 18 and the other ingredients (saccharin and Mg stearate) were added to them. The granule mixtures were compressed into tablets by using a single-punch press machine. Prepared tablets were wrapped in aluminum foil and were packaged in plastic tubes.

### 2.4. Physicochemical Evaluation of Effervescent Granule of Jicama Extract

The granule physicochemical evaluation involved was organoleptic, Hausner's ratio, angle of repose, compressibility index, moisture content, and particle size determination. *Organoleptic* was observed as its odor, color, and flavour. For evaluation of powder flow, the Hausner's ratio, angle of repose, and compressibility index can be used. *Angle of repose* ( $\theta$ ) is constant angle that occurs between the deposited particles cone shape with a horizontal plane if a certain amount of granule is poured into the apparatus gauge.

TABLE 1: Effervescent Tablet Formulation of Jicama Extract.

| Ingredients             | Concentration (%) |       |       |       |
|-------------------------|-------------------|-------|-------|-------|
|                         | F1                | F2    | F3    | F4    |
| Jicama extract          | 12.5              | 12.5  | 12.5  | 12.5  |
| PVP 40                  | -                 | -     | 0.75  | 0.75  |
| Gelatin                 | 0.75              | 0.75  | -     | -     |
| Citric acid             | 7                 | 7     | 7     | 7     |
| Tartaric acid           | 10                | 10    | 10    | 10    |
| Sodium bicarbonate      | 20                | 20    | 20    | 20    |
| Lactose                 | 47.75             | -     | 47.75 | -     |
| Mannitol                | -                 | 47.75 | -     | 47.75 |
| Mg stearate             | 1                 | 1     | 1     | 1     |
| Saccharin               | 1                 | 1     | 1     | 1     |
| Orange flavouring agent | qs                | qs    | qs    | qs    |

A good angle of repose is between 25-40° (14). Angle of repose was determined by equation 1.

$$\tan(\alpha) = \frac{\text{height}}{0,5 \text{ diameter}} \quad (1)$$

*Compressibility Index and Hausner's Ratio* was measured for bulk density and tapped density. Bulk density was measured by pouring 100 grams of granules into the graduated cylinder (250 ml) using a glass funnel and its volume is recorded (13).

$$\rho_{\text{bulk}} = \frac{m}{V_{\text{bulk}}} \quad (2)$$

After measuring the bulk volume, the same measuring cylinder was subjected to 500 & 1250 mechanical taps with the help of a mechanical tapping machine (tapped density measuring apparatus). After tapping, the volume was again measured as ml or cc, which is called as tapped volume and the tapped density is calculated by the following equation (15).

$$\rho_{\text{tapped}} = \frac{m}{V_{\text{tapped}}} \quad (3)$$

*Compressibility Index* can be calculated from the following equation (15).

$$\text{Compressibility index} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \quad (4)$$

and *Hausner's ratio* can be calculated by the following equation (15).

$$\text{Hausner's ratio} = \frac{\text{Tapped density}}{\text{Bulk density}} \quad (5)$$

*Moisture content* was measured by using moisture balance. 1 gram granule was put in the machine and measure the water content by pressing the start button to get the

percent water content. Measurements were carried out until a constant moisture content was obtained for 3 measurements. Good moisture content for effervescent granule is 1-2% (16).

*Particle size* was measured by using sieve shaker. 100 grams of granules poured on the upper sieve and was passed through a series of the sieves i.e.20, 30, 40, 50, 60, 80, and 100. The apparatus was shaking for 10 minutes. The amount remaining on each sieve was weighed and percentage of granules retained on each sieve was calculated using the initial weight taken. The mean diameter of the granules was calculated by following equation (13).

$$d = \sum \frac{X_i d_i}{100} \quad (6)$$

$x_i$  = The average size of both upper and lower sieve

$d_i$  = The percentage of the amount of  $i$  in limited area by two sieves

All measurements was interpreted according to USP 44 NF 39 (17).

## 2.5. Physicochemical Evaluation of Effervescent Tablet of Jicama Extract

The tablet physicochemical evaluation involved was weight variation, thickness, hardness test, friability test, pH, and effervescence time. *Tablet weight variation* was determined using analytical balance. 20 tablets were taken each time and weighed accurately to determine the weight variation. *Tablet thickness* was measured using vernier calipers for 10 tablets from each formulation. *Tablet hardness* was determined for 10 tablets of each formulation by using a hardness tester. Hardness of effervescent tablets is usually lower than conventional tablets and minimum of acceptable hardness of uncoated tablets is 40 N approximately. *Tablet friability* was evaluated using friability tester. 20 tablets of each formulation was taken randomly and after weighting altogether, were placed in the friabilator chamber for 4 minutes at 25 rpm. *pH solution of tablet* was determined with one tablet in 200 ml of purified water at  $20 \pm 1^\circ\text{C}$  by using pH meter, immediately after completing the dissolution time. *Effervescence time* was calculated by placing a single tablet in a beaker containing 200 ml of purified water at  $20^\circ\text{C} \pm 1^\circ\text{C}$ . Whenever a clear solution without particles was obtained effervescence time has finished (13,15,17).

## 3. RESULTS AND DISCUSSION

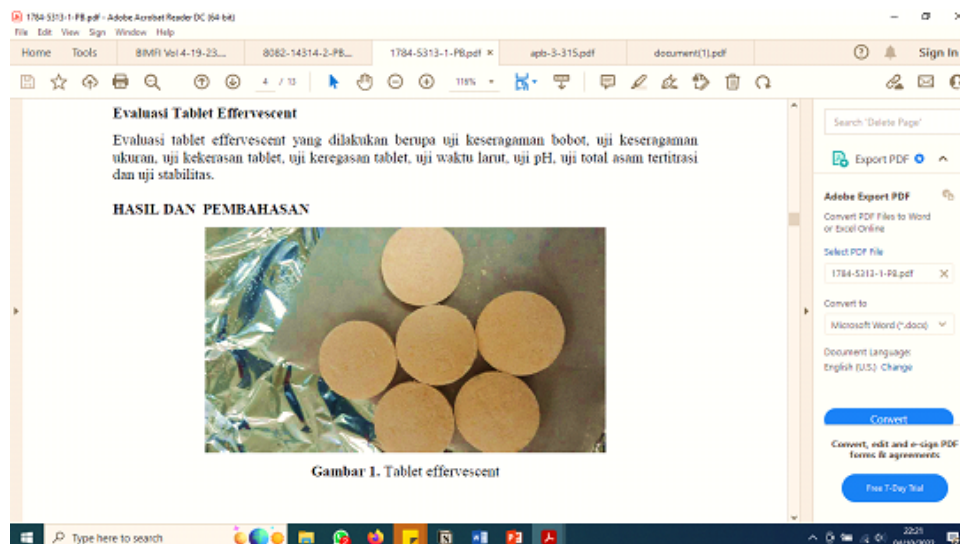


Figure 1: Effervescent Tablet of Jicama Extract.

### 3.1. Physicochemical Evaluation of Effervescent Granule of Jicama Extract

Organoleptic test was carried out to see the physical appearance of the preparation by observing the color, odor and flavour of the preparation. The all effervescent granule are orange in color, have no odor, and has a sweet flavour. This is in accordance with the initial specifications of the tablet.

TABLE 2: Physicochemical Evaluation of Effervescent Granule of Jicama Extract.

| Granule Characteristics   | F1          | F2          | F3          | F4          |
|---------------------------|-------------|-------------|-------------|-------------|
| Hausner's Ratio           | 1.15±0.02   | 1.12±0.01   | 1.13±0.03   | 1.08±0.01   |
| Angle of Repose (°)       | 35.12±1.76  | 31.05±1.23  | 31.78±0.95  | 27.64±1.43  |
| Compressibility Index (%) | 14.35±0.57  | 11.71±0.43  | 12.33±0.82  | 9.36±0.75   |
| Moisture Content (%)      | 1.30±0.03   | 1.24±0.01   | 1.25±0.02   | 1.28±0.01   |
| Mean Particle Size (µm)   | 351.3±17.91 | 332.7±23.06 | 306.4±27.45 | 305.1±14.67 |

Flowability is an important bulk powder characteristic. The term “flowable” means an irreversible deformation of a powder to make it flow due to the application of external energy or force. Various parameters such as angle of repose, Carr’s compressibility index, and Hausner ratio are used to express flowability of powders. It can be used to predict the propensity of a given powder sample to be compressed, and which are understood to reflect the importance of interparticulate interactions (18,19). The result of Hausner’s ratio, angle of repose, compressibility index, moisture content and mean particle size measurement was done in triplicate and average values calculated (Table 2). Based on scale of flowability (Table 3) (18), it can be seen that the resulting granules



have good flow properties for F1-F3 and excellent flow properties for F4. This is because PVP is a material with good flow properties (20) and its flowability increases as the moisture content decreases, due to an decrease in cohesion from stronger interparticle liquid bridges (21). This material is combined with mannitol which has small particle size and showed quite high flowability. The spherical shape of granules effectively improved the flowability of mannitol. In addition, low humidity also reduces poor flow properties (22,23).

TABLE 3: Scale of Flowability.

| Flow character  | Compressibility index | Hausner ratio | Angle of Repose |
|-----------------|-----------------------|---------------|-----------------|
| Excellent       | ≤ 10                  | 1.00-1.11     | 25-30           |
| Good            | 11-15                 | 1.12-1.18     | 31-35           |
| Fair            | 16-20                 | 1.19-1.25     | 36-40           |
| Passable        | 21-25                 | 1.26-1.34     | 41-45           |
| Poor            | 26-31                 | 1.35-1.45     | 46-55           |
| Very poor       | 32-37                 | 1.46-1.59     | 56-65           |
| Very, very poor | >38                   | >1.60         | >66             |

Moisture is related to the stability of the effervescent tablets produced. The higher the humidity, the more difficult it is tableting because with high humidity the acid-base in the tablets will react more quickly so that the resulting tablets will become soft more quickly (24). From Table 2, it can be seen that moisture content of four formulas meet the requirement.

In producing direct compression method, the mixtures of powder with excellent flowability, and without particles segregation are needed and particle size of all raw materials should be equal. It is necessary to prepare granules, if particle size is small (13). From Table 2, it can be seen that the particle size is small for all formula and F4 has the smallest mean particle size.

### 3.2. Physicochemical Evaluation of Effervescent Tablet of Jicama Extract

Dosage uniformity can be determined by the weight variation test. This requirement applies to preparations containing one active substance and preparations containing two or more active substances (20). The average percentage weight of the tablets in all formulas are meet the requirement. Likewise, the tablet thickness test has met the requirements of the Farmakope Indonesia.

TABLE 4: Physicochemical Evaluation of Effervescent Tablet of Jicama Extract.

| Tablet Characteristics | F1        | F2        | F3        | F4        |
|------------------------|-----------|-----------|-----------|-----------|
| Weight Variation (%)   | 1.03±0.01 | 1.24±0.05 | 1.15±0.01 | 1.21±0.03 |
| Thickness (mm)         | 6.05±0.01 | 6.15±0.02 | 6.03±0.02 | 6.24±0.01 |
| Hardness (kg)          | 9.20±1.65 | 5.40±1.35 | 8.80±0.95 | 4.40±1.45 |
| Friability (%)         | 0.66±0.13 | 0.93±0.13 | 0.81±0.09 | 1.12±0.11 |
| pH solution            | 5.32±0.04 | 5.46±0.01 | 5.28±0.04 | 5.37±0.03 |
| Effervescence Time (s) | >240      | 145±3.75  | 220±2.13  | 96±3.85   |

Hardness of effervescent tablets is usually lower than conventional tablets and minimum of acceptable hardness of uncoated tablets is 40 N or 4kg approximately (13). Tablet hardness directly affects tablet friability and effervescence time. The higher the tablet hardness, the lower the tablet friability and the longer the effervescence time. This theory is in accordance with the results in Table 4. pH solution of tablet less than 6 is necessary to increase the absorption of effervescent tablets, that pH of four formulations are less than 6. In other study on effervescent granules containing citric acid and sodium bicarbonate has been done, solution pH which is obtained from dissolving granules was measured at 5.64. It is comparable with the results in this study (13).

Effervescence time was strongly influenced by the percentage of sodium bicarbonate in the effervescent mixture and by the particle size. The interaction between these factors was statistically significant with a positive term, indicating that both factors combined to promote an increase in the disintegration time. A high concentration of sodium bicarbonate reduces the disintegration time, favoring effervescence (negative term in the equation). Furthermore, the particle size increases the disintegration time, making effervescence slow (positive term of the equation) (25).

## 4. CONCLUSION

Among the studied formulations, formula 4 with combination of PVP 40 as binder and mannitol as diluent produced optimum formula for jicama extract. F4 was desirable for all physiochemical characteristics, including excellent granule flowability, low moisture content and small particle size, low weight and thickness variation, hardness about 4kg, pH <6, and effervescent time under 3 minutes. Ethanol extract of jicama can be formulated into effervescent tablet and has potential to be developed as a treatment for osteoporosis. We suggest for continuing research on the in vitro and in vivo effectiveness.

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