Design, Formulation and Tableting Properties of Aqueous Leaf Extract of *Moringa oleifera*

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**Authors’ contributions**

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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**ABSTRACT**

**Aim:** The aim of this study is to formulate a standard dose of aqueous extract of *Moringa oleifera* leaves into tablets and to determine a suitable binder for the formulation.

**Methodology:** Aqueous extract of *Moringa oleifera* leaves was extracted and formulated using different binders which included Maize Starch, Gelatin and Micro-crystalline Cellulose (MCC) to find out which one produce better tablets of aqueous extract of *Moringa oleifera* leaves. Formulations were characterized using various parameters such as physicochemical properties (bulk density, tapped density, moisture content, Hausner’s...
ratio, Carr’s index, ash value), strength (friability and crushing strength) and release properties (disintegration and dissolution times tests). The result showed that tablets formulated with Gelatin as a binder has lowest friability and disintegration time compared to those formulated with either MCC or maize starch. The crushing strengths were all within the acceptable limit (3 – 6 KgF) except maize starch which was higher. **Conclusion:** *Moringa oleifera* tablets were successfully formulated and based on experiments conducted, Gelatin is preferable in the formulation of *Moringa oleifera* tablets.

**Keywords:** *Moringa oleifera*; tablet; binder; maize starch; gelatin; MCC.

### 1. INTRODUCTION

*Moringa oleifera* is one of the widely distributed and naturalised species of a monogeneric family *Moringaceae* [1] which includes 13 species of trees and shrubs distributed in sub-Himalayan ranges of India, Sri Lanka, Africa and Arabia [2]. The tree ranges in height from 5 to 10m [3] and is found wild and cultivated throughout the plains especially in hedges and in house yards.

It is rich in number of vitamins and minerals as well as other phytochemicals including carotenoids. The stem bark is reported to contain two alkaloids namely: moringine and moringinine [4]. Vanillin, beta sitosterol, beta sitostenone, 4-hydroxymellin and octacosonoic acid have been isolated from the stem of the plant [5]. Flowers contains 9 amino acids, sucrose, D-glucose, traces of alkaloids, wax, quercetin and kaempferat. They have also been reported to contain some flavonoid pigments such as kaempferol, rhamnet, isoquerzetin and kaempferitin [5].

The leaves are the most nutritious part of the plant being a significant source of vitamin B6, C, provit A as beta carotene, magnesium and protein among other nutrients [6]. *Moringa* has been used in folk medicine including ayurvedic traditional medicine. A number of medicinal properties have been ascribed to various parts of this tree for use in various ailments [7].

It is used to treat several diseases such as infection, urinary tract infection, Epstein-Bar virus (EBV), Herpes simplex virus (HSV-1), HIV-AIDS, hepatitis, helminthes, trypanosomes, bronchitis, external sores/ulcers and fever. It has anti-tumor, prostate, radio protective, anti-anemic, antihypertensive, antidiabetic, diuretic, antioxidant and antiseptic activities. The plant was reported to be used in treatment of hypercholesteremia, thyroidism, colitis, diarrhea, dysentery, ulcer/gastritis, rheumatism, headache, iron deficiency, vitamin/mineral deficiency, enhance lactation, catarrh, malnutrition, weight reduction and scurvy [2,7-11].

The leaf was certified safe by many authors [12] when used for a short term. However, organ toxicities have been reported when the leaves are used for long period [2,10,13]. Fifty milligrams dose was chosen for the formulation because it was earlier documented that the acute toxicity (LD$_{50}$) of aqueous extract of 16.1 g/kg [10]. The leaves are mostly soaked in water or alcohol (ethanol) locally before use in treatment of diseases. Difficulties are usually encountered in formulation of powdered leaves [14] probably because of presence of other matters. Therefore, aqueous leaf extract was chosen for the study. Herbs have been formulated into various dosage forms for easy administration as well to standardize the dose of the formulation such as herbal tablets containing *Ipomea digitata* [15].
The aim of this study is to formulate a standardized amount of aqueous extract of *Moringa oleifera* leaves to tablets and to determine suitable binder for the formulation, so that it would serve as an alternative dosage form in which *Moringa oleifera* can be used.

2. MATERIALS AND METHODS

2.1 Materials

*Moringa oleifera* extract from *Moringa oleifera* leaves, Magnesium stearate (BDH chemicals, Pooles, England), Talc (BDH chemicals, Pooles, England), Lactose (BDH chemicals, Pooles, England), Micro crystalline Cellulose (BDH chemicals, Pooles, England), Gelatin (BDH chemicals, Pooles, England). The reagents were purchase from a commercial source in Kano, Nigeria.

2.2 Methods

2.2.1 Collection and identification of *Moringa oleifera*

*Moringa oleifera* leaves were obtained from Yankaba market in Kano, Kano state, Nigeria and were transported in a woven cotton sack via road to Maiduguri, Borno state, Nigeria within 4 hours. It was later authenticated by a taxonomist from the Department of Biological Sciences, University of Maiduguri, Nigeria. The plant specimen was deposited in herbarium and specimen voucher number 1401C was obtained for further reference.

2.2.2 Extraction of *Moringa oleifera* leaves

The fresh *Moringa* leaves were shade dried in the Pharmaceutics laboratory for 3 days. The stalks were removed and the leaves were size reduced using a mortar and pestle. The weight of dried powder was noted. An aqueous extract was obtained using the rotary extractor thermostatically maintained at 55°C and was dried for 3 days at room temperature. The extract was weighed then size reduced using a porcelain mortar and pestle and the percentage yield was calculated. The powder was sieved and the fraction that passed through 180 µm sieve was used for the study.

2.2.3 Characterization of *Moringa oleifera* powder

2.2.3.1 Moisture content

The moisture content of *Moringa oleifera* powder was determined using a moisture analyser (Sartorius, Germany) as earlier described by Madu [16]. 3 g weight of the powder was poured into the moisture balance and evenly distributed on the tray. The machine was set at 130±1°C. The readings were noted when the machine automatically stops. The experiment was repeated twice and the average of the three readings was taken as the moisture content.

2.2.3.2 Angle of repose

The angle of repose of the powder was determined using a glass funnel clamped on a retort stand which is 10cm away from the flat surface of the bench. 30g weight of the powder was
placed into the funnel and allowed to flow freely forming a conical heap. The angle of repose was calculated from the heap of the powder using the formula;

\[
\tan \theta = \frac{h}{r}
\]  

(1)

Where \( h \) = height of the heap and \( r \) = radius of the circular heap.

The experiment was repeated twice and the average of the three readings was taken as the angle of repose.

2.2.3.3 Bulk and tapped densities

This was carried out by measuring the volume occupied by a 30g weight of the powder in a dry measuring cylinder. The bulk density \( B_d \) was calculated using the formula:

\[
B_d = \frac{W_p}{V_p}
\]  

(2)

Where \( W_p \) = Weight of the powder, \( V_p \) = Volume occupied by the powder

The measuring cylinder was then tapped 50 times on a wooden table from a height of about 2cm and the tapped volume was recorded. The tapped density \( T_d \), was calculated thus:

\[
T_d = \frac{W_p}{T_v}
\]  

(3)

Where \( T_v \) = Tapped volume occupied by Moringa powder

The experiment was repeated twice and the average of the three readings was taken as the value of bulk and tapped densities.

2.3 Determination of Carr’s Index

Carr’s index \( CI \), was calculated from the results obtained from bulk and tapped densities above using the relation;

\[
CI = \left( T_d - B_d \right) \times \frac{100}{T_d}
\]  

(4)

2.4 Determination of Hausner’s Ratio

Hausner’s ratio \( HR \), was determined using the results obtained from both bulk and tapped densities. It was calculated using the formula;

\[
HR = \frac{T_d}{B_d}
\]  

(5)

2.5 Ash Value

The method of Momin and Kadam [17] was used with slight medication. 2g weight of the powder sample was poured into a nickel crucible which was initially heated at 105°C to a
constant weight and allowed to cool. The crucible with its content was then gently heated until it was moisture free and completely charred. The heat was increased gradually until most of the carbon vaporised. The sample was finally heated strongly at 600 °C until the residue is free from carbon (i.e. almost white). The crucible with its content was allowed to cool and weighed. The heating and cooling step was then repeated until the residue (ash) was constant.

The weight of the ash was then determined and the percentage ash value calculated

\[
\% \text{ Ash value} = \frac{W_a \times 100}{W_{sp}}
\]

Where \( W_a \) and \( W_{sp} \) are weight of ash formed and initial weight of \( Moringa \) powder respectively.

2.6 Preparation of the \textit{Moringa} granules

The \textit{Moringa} granules were prepared by the wet granulation method according to the working formula in (Table 1).

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Binders</th>
<th>Maize Starch (F1)</th>
<th>MCC (F2)</th>
<th>Gelatin (F3)</th>
<th>Control (F4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>\textit{Moringa} extract (mg)</td>
<td>50.0</td>
<td>50.0</td>
<td>50.0</td>
<td>50.0</td>
<td>50.0</td>
</tr>
<tr>
<td>Lactose (mg)</td>
<td>86.5</td>
<td>86.5</td>
<td>89.7</td>
<td>94.5</td>
<td></td>
</tr>
<tr>
<td>Maize Starch (mg)</td>
<td>12.0</td>
<td>12.0</td>
<td>12.0</td>
<td></td>
<td>12.0</td>
</tr>
<tr>
<td>Binder (mg)</td>
<td>8.0</td>
<td>8.0</td>
<td>4.8</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Talc (mg)</td>
<td>3.2</td>
<td>3.2</td>
<td>3.2</td>
<td>3.2</td>
<td></td>
</tr>
<tr>
<td>Mg Stearate (mg)</td>
<td>0.3</td>
<td>0.3</td>
<td>0.3</td>
<td>0.3</td>
<td></td>
</tr>
<tr>
<td>Theoretical Weight (mg)</td>
<td>160.0</td>
<td>160.0</td>
<td>160.0</td>
<td>160.0</td>
<td></td>
</tr>
</tbody>
</table>

Key: MCC = Microcrystalline Cellulose

The formulations (F1 to F4) contain 12 mg maize starch each as disintegrant. The disintegrants were incorporated intra-granularly. In addition, maize starch was also used as binder in F1.

Weighing: 50 g of \textit{Moringa oleifera} powder, 86.5 g of lactose and 12 g of maize starch were weighed.

Mixing: The batches were small (1000 tablets per batch), mixing was done for 10 min, the extract and other excipients were mixed thoroughly.

Preparation of binder solution: 5% w/w of starch paste was prepared by weighing 5 g of binder maize starch powder and dispersed into 30 ml of distilled water. It was then added to a boiling distilled water placed on a hot plate (Harry Gestigkeit, Germany) with continuous stirring until translucent paste was formed. The final 100 ml mark was made with distilled water and allowed to cool.

Addition of binder: Small quantity of the paste was added gradually to the powder mixture until moistened mass was formed.
Wet screening: The moistened mass was passed through a 1.7 mm sieve.
Drying: The wet granules were dried in a hot air oven (Venticell, Germany) at 40°C.
Dry screening: The granules were then passed through 1.4 mm sieve and oversize granules were size reduced. Same was done for F3 but for F2, MCC was added in dry form. For F4 distilled water was used instead of binder solution. The granules were then characterized.

2.7 Granule Characterization

The following tests (Angle of repose, Bulk density, Tapped density and Moisture content) were carried out as earlier described for Moringa powder on the granules produced prior to compression into tablets.

2.8 Compression of Granules into Tablets

The granules were then mixed with talc and magnesium stearate prior to compression. The granules were compressed into tablets on single punch tablet press (Manesty F3, England), using die and flat punch set of diameter 8 mm at compressional force of 6 metric tons to produce circular tablets.

The tablets were kept in air tight containers for 48 hr prior to quality control tests.

3. QUALITY CONTROL ON THE FORMULATED TABLETS

3.1 Uniformity of Thickness and Diameter

Vernier Calliper (Moore and Wright, England) was used to measure the diameter and thickness of the tablets. The mean value of five determinations was recorded in each case. The experiment was repeated twice and the average of the three readings was taken as the thickness/diameter.

3.2 Uniformity of Weight Test

Twenty tablets were randomly selected and weighed individually. The mean weight of the tablets was then calculated and the standard deviation determined.

3.3 Crushing Strength

The Erweka hardness tester was used in measuring the hardness of the tablets. Six tablets were selected at random and each tablet was in turn placed between the anvil and the spindle of the hardness tester (Erweka TBH 100, Germany) and subjected to increasing pressure by turning the knurled knob in a clockwise direction at constant rate until the tablet was crushed. The value of the pressure applied (KgF) was taken as the Crushing Strength of the tablet. The mean of six determinations were taken.

3.4 Friability Test

Twenty tablets were randomly selected and weighed accurately. They were then placed inside the drum of Friabilator (Erweka, Germany) and operated for four minutes at a speed
of 25 rpm. The intact tablets were removed from the drum, dusted and weighed. The percentage loss in weight was calculated and recorded as friability value.

### 3.5 Disintegration Time Test

Six tablets were randomly selected and placed individually in the six tubes of the rack of the disintegrating machine (Erweka ZT-71, Germany). The rack was then raised and lowered at constant rate in distilled water contained in a glass jar suspended in a water bath whose temperature was thermostatically maintained at 37±1°C. The time taken for the last tablet or its fragment to pass through the 2mm mesh into the disintegrating medium (distilled water) was recorded as the disintegration time.

### 3.6 Dissolution Time Test

The calibration curve was constructed using the *Moringa oleifera* extract and 0.1M HCl as the dissolving medium, 10mg of the extract was weighed and diluted in 150 ml of 0.1M HCl 0.5, 1.0, 1.5, 2.0, 2.5ml of the stock was then re-diluted in 5 ml volumetric flask to give 6.66, 13.33, 20, 26.67, 33.33µg/ml concentrations respectively. The absorbance of the different concentrations was spectrophotometrically determined at 205.1nm wavelength using a UV spectrophotometer (6405 UV/Vis Barlowond scientific, UK) and a graph of absorbance against concentration was plotted.

The Dissolution test apparatus (Erweka DT 700, Germany) was used to determine the dissolution rate of the *Moringa* tablets. The dissolution medium used was 750 ml 0.1M HCL, thermostatically maintained at 37±0.5°C. The paddle was set to rotate at 50rpm. One tablet was placed into each glass jar. Samples of the dissolution medium (10ml) were then withdrawn at specified time interval of 15, 30, 45, 60 min respectively and analysed at 205.1nm using UV Spectrophotometer (6405 UV/Vis Barlowond scientific, UK). After each withdrawal of the sample, same volume of fresh dissolution medium was replaced.

### 3.7 Statistical Analysis

Statistical analysis was carried out using a statistical software SPSS [18] version 16 and p<0.05 was considered significant.

### 4. RESULTS AND DISCUSSION

#### 4.1 Characterization of Powder

The percentage yield of the *Moringa* powder obtained from the fresh leaves of *Moringa oleifera* (Table 2) shows a relatively high yield. This is good as the tree is found in the wild as well as cultivated and can produce leaves throughout the year [19].

The moisture content for the *Moringa oleifera* extract as shown in (Table 2) is low which indicates that it has less risk of microbial contamination and also prevents the growth of moulds and fungi.

Angle of repose is used to measure the flow property of the powder with values less than 23° having the best flow while values ranging from 23-25° has good flow [20]. *Moringa* extract showed good flow property.
Moringa powder also has a bulk and tapped densities as shown in (Table 2) which is suggestive of good flow property.

Hausner’s ratio also measures the flow property of powder and values less than 1.25 indicates a good flow property [20] and as shown in (Table 2), Moringa extract has a value of 1.23 which indicates good flow ability.

For Carr’s index, values below 16 indicate good flow property [20]. Moringa extract has slightly higher value.

Table 2. Physicochemical properties of Moringa oleifera powder

<table>
<thead>
<tr>
<th>S/no</th>
<th>Parameters</th>
<th>Moringa oleifera powder</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Moisture content (%)</td>
<td>2.84±0.64</td>
</tr>
<tr>
<td>2</td>
<td>Angle of repose (°)</td>
<td>23.90±1.37</td>
</tr>
<tr>
<td>3</td>
<td>Bulk density (g/ml)</td>
<td>0.99±0.04</td>
</tr>
<tr>
<td>4</td>
<td>Tapped density (g/ml)</td>
<td>1.22±0.12</td>
</tr>
<tr>
<td>5</td>
<td>Carr’s index (%)</td>
<td>18.90±0.93</td>
</tr>
<tr>
<td>6</td>
<td>Hausner’s ratio</td>
<td>1.23±0.08</td>
</tr>
<tr>
<td>7</td>
<td>Ash value</td>
<td>0.23±0.23</td>
</tr>
<tr>
<td>8</td>
<td>Percentage Yield (%)</td>
<td>13.25±1.09</td>
</tr>
</tbody>
</table>

The ash value of Moringa extract as shown in (Table 2) indicates that there is the presence of organic salts e.g. calcium oxalate found naturally in drugs as well as inorganic matter derived from external sources. Ash value test is one of the most important tests in the examination of powdered drugs.

4.2 Characterisation of Granules

(Table 3) shows the results of various tests carried out on the granules produced using different binders.

Table 3. Physicochemical properties of Moringa granules

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Angle of repose (°) ±SD</th>
<th>Bulk Density (g/ml) ±SD</th>
<th>Tapped density (g/ml) ±SD</th>
<th>Carr’s index ±SD</th>
<th>Hausner’s ratio ±SD</th>
<th>Moisture content ±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>15.06±0.28</td>
<td>1.08±0.023</td>
<td>1.23±0.03</td>
<td>12.2±0.06</td>
<td>1.14±0.01</td>
<td>1.77±0.01</td>
</tr>
<tr>
<td>F2</td>
<td>22.52±1.10</td>
<td>0.59±0.014</td>
<td>0.66±0.01</td>
<td>9.2±0.01</td>
<td>1.10±0.01</td>
<td>2.00±0.01</td>
</tr>
<tr>
<td>F3</td>
<td>22.10±0.58</td>
<td>0.61±0.022</td>
<td>0.65±0.01</td>
<td>6.2±0.01</td>
<td>1.07±0.01</td>
<td>1.58±0.01</td>
</tr>
<tr>
<td>F4</td>
<td>18.24±0.90</td>
<td>0.61±0.004</td>
<td>0.65±0.01</td>
<td>6.15±0.01</td>
<td>1.07±0.01</td>
<td>1.65±0.02</td>
</tr>
</tbody>
</table>

Key F1=maize starch, F2=MCC, F3=Gelatin and F4=control; MCC = Microcrystalline cellulose

The flow properties of the granules were generally better than those of Moringa powder. This can be explained the presence of binder tends to produce denser granules which are larger than the powder particles. The larger the size of powder particle, the smaller the surface activity and hence the better flow [21]. Although all the binders fall within the normal range of below 23° [20], the best binder to use is maize starch because it has the lowest value which indicates a better flow ability than the rest of the binders.
4.3 Quality Control of Formulated Tablets

(Table 4) shows the results of the quality control tests carried out on Moringa tablets produced with different binders. The tablets have uniform diameter and thickness which conforms to the specification which states that the range of tablet thickness should be between ±5% [22]. The result of the uniformity of weight (Table 4) as observed showed that the tablets have a standard deviation of less than 0.1 which conforms to the standard set by the USP [23] which stipulates that the limit should not exceed 7.5% for tablets weighing between 130-324 mg.

Table 4. Physicochemical properties of the Moringa oleifera tablets

<table>
<thead>
<tr>
<th>Parameter</th>
<th>MCC</th>
<th>Maize starch</th>
<th>Gelatin</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thickness (mm)</td>
<td>5.12±0.15</td>
<td>5.09±0.06</td>
<td>5.04±0.11</td>
<td>4.98±1.27</td>
</tr>
<tr>
<td>Diameter (mm)</td>
<td>8.03±0.18</td>
<td>8.17±0.58</td>
<td>8.10±0.03</td>
<td>8.09±0.43</td>
</tr>
<tr>
<td>Weight (g)</td>
<td>0.163±0.03</td>
<td>0.154±0.01</td>
<td>0.155±0.01</td>
<td>0.157±0.01</td>
</tr>
<tr>
<td>Crushing strength (Kg/F)</td>
<td>4.06±0.43</td>
<td>7.20±0.19</td>
<td>4.5±0.15</td>
<td>3.64±0.02</td>
</tr>
<tr>
<td>Friability test (%)</td>
<td>0.38±0.01</td>
<td>0.39±0.04</td>
<td>0.24±0.05</td>
<td>0.25±0.18</td>
</tr>
<tr>
<td>Disintegration time (min)</td>
<td>21.96±0.40</td>
<td>17.59±0.40</td>
<td>11.64±0.80</td>
<td>11.63±0.80</td>
</tr>
<tr>
<td>CSFR</td>
<td>10.68</td>
<td>18.46</td>
<td>17.85</td>
<td>14.56</td>
</tr>
<tr>
<td>CSFR-DT</td>
<td>0.49</td>
<td>1.05</td>
<td>1.61</td>
<td>1.25</td>
</tr>
</tbody>
</table>

Key: CSFR = Crushing Strength Friability Ratio, DT = Disintegration Time

All the formulations fall within the acceptable crushing strength range of 3-6 KgF [24] except F1 (when maize starch was used as binder). There was significant difference between F4 (control) and either F1, F2 or F3 (p<0.05). From the friability test as shown in the (Table 4), all the tablets fall within acceptable compendial [25] range. There was no significant difference between F4 and F3 (p>0.05) but there was significant difference between F4 and either F1 or F2 (p<0.05). Therefore, the best formulation is F3 (i.e the binder of choice is Gelatin) because it has good impaction ability and is less friable. It is pertinent to note that formulation F4 containing no binder passed both friability and crushing strength tests. It was as a result of proportion of the starch added as disintegrant being wetted in the process of granulation thereby acting as binder.

As shown in (Table 4), Gelatin has the highest disintegration time probably because it has a lower concentration of binder. As a result, it is preferable in the production of Moringa tablets because it has a better disintegration profile which is the rate determining step in drug absorption [26]. There was significant difference between F4 and either F1 and F2 (p<0.05) but there was no significant difference between F4 and F3 (p>0.05).

The values of crushing strength and friability provide measures of tablet strength and weakness, respectively. Thus, the CSFR can be used as a measure of the mechanical strength of the Moringa tablets, the higher the CSFR, the stronger the tablets. The result of CSFR showed tablets produced with gelatin as binder has better mechanical strength. The ranking is gelatin>maize starch>MCC.

The effects CSFR on disintegration time of the tablets has also followed same pattern. The CSFR-DT values ranking was gelatin>maize starch>MCC for the Moringa tablets. This is an indication that gelatin is better binder to be used in the formulation of the Moringa tablets.
Dissolution is the time taken for a tablet to go into solution and a tablet must first disintegrate before it goes into solution [26]. (Fig. 1) illustrates the dissolution profile of the various tablets containing different binders with Gelatin having the best dissolution profile (up to 100%) and therefore, can be declared as the better binder in the production of *Moringa oleifera* tablets. However, it should be noted that a tablet can disintegrate rapidly but still have delayed dissolution profile due to the fact that it can actually disintegrate into hard coarse particles from which dissolution may be slow [26].

**Fig. 1.** Dissolution profile of various binders used in tableting *Moringa oleifera*

*Key: F1 = Maize starch, F2 = Microcrystalline cellulose, F3 = Gelatin and F4 = Control*

5. CONCLUSION

A 50 mg *Moringa oleifera* tablet was successfully formulated from aqueous extract of *Moringa oleifera* leaves. It can therefore be concluded that *Moringa oleifera* can be tableted using different binders and still get promising results. Based on experiments conducted, the binder of choice for producing *Moringa oleifera* tablets is Gelatin as it has passed all the tests required. Further studies should be carried out on Mechanical Strength and Lamination tendencies of *Moringa* tablets.
CONSENT
Not applicable.

ETHICAL APPROVAL
Not applicable.

COMPETING INTERESTS
Authors have declared that no competing interests exist.

REFERENCES

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