

FORMULATION AND EVALUATION OF ANTITUMOR ACTIVITY OF *ARTEMISIA ARBORESCENCE* EXTRACT CAPSULES AS DIETARY SUPPLEMENTS HERBAL PRODUCT AGAINST BREAST CANCER

Prof. Dr. Mahmoud Mahyoob Alburyhi^{1,2*} and Prof. Dr. Amina El-Shaibany³

¹Professor Dr. of Pharmaceutics and Industrial Pharmacy, Department of Pharmaceutics and Industrial Pharmacy, Faculty of Pharmacy, Sana'a University, Sana'a, Yemen.

²Head of Department of Pharmacy, Faculty of Medicine and Health Sciences, AlJeel AlJadeed University, Yemen.

³Professor Dr. of Pharmacognosy, Department of Pharmacognosy, Faculty of Pharmacy, Sana'a University, Sana'a, Yemen.

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*Corresponding Author

Prof. Dr. Mahmoud
Mahyoob Alburyhi

Professor Dr. of
Pharmaceutics and
Industrial Pharmacy,
Department of
Pharmaceutics and
Industrial Pharmacy, Faculty
of Pharmacy, Sana'a
University, Sana'a, Yemen.

ABSTRACT

Artemisia arborescence plant widely distributed in Yemen, traditionally used to treat dermatitis, allergic reactions, itchiness lymphatic drainage, venous congestions Asthma, hay fever, asthmatic bronchitis. The essential oil of this plant was traditionally used as an insect repellent, as flavourings and for fragrances. Inhalation of the oil is used to dilate and stimulate the bronchi, blood vessels of the heart and to stimulate the kidneys. The oil is for inhalation only. *Artemisia arborescence* has been used traditionally as an anti-inflammatory remedy. The essential oil of *Artemisia arborescence* has been reported to have antibacterial and antifungal activities as well as antiviral activity against HSV-1 and HSV-2. *Artemisia arborescence* essential oil also exhibited antifungal activity against *Cladosporium cucumerinum*. The antitumor activity of *Artemisia arborescence* can be attributed to the presence of α -bisabolol and palmitic acid. *Artemisia arborescence* is commonly used in traditional medicine for a wide range of ailments including gastritis and gastric ulcer. Food poisoning commonly caused by salmonella typhimurium pathogenic gram-negative short rods. *Artemisia arborescence* is commonly used in

traditional medicine for a wide range of ailments including gastritis, gastric ulcer and food poisoning. The antitumor activity of ethanol extract of *Artemisia arborescence* was evaluated at the dose of 100mg/kg and showed a significant activity for breast cancer. *Artemisia arborescence* was formulated as capsules and evaluate for organoleptic properties of ethanol extract of *Artemisia arborescence*. The results show that the extract was the best formulation F4 according to dissolution was 96.6% after 45 min, and stability under various storage condition were evaluated.

KEYWORDS: *Artemisia arborescence*, Extract, Capsules, Herbal medicines, Breast cancer, Antitumor activity.

INTRODUCTION

There has been a great interest in the last few decades in using plants to cure diseases in general, and to consider it as a main source in the alternative medicine to cure the chronic diseases in particular.^[1] Prescriptions that contain compounds refer to chemical groups produced by plants are called botanical products.

According to the World Health Organization (WHO), "Herbal Preparations" contain plant parts or plant material in the crude or processed state as active ingredients and may contain excipients (foreign substances).^[2] Combinations with chemically defined active substances or isolated constituents are not considered herbal preparations.^[3]

Plant medicines are generally considered to be safer and less damaging to the human body than synthetic drugs. Furthermore, there is a current upsurge of interest in plants that is further supported by the fact that many important drugs in use today were derived from plants or starting molecules of plant origin: Digoxin / Digitoxin, the Vinca Alkaloids, Reserpine and Tubocurarine are some important examples.^[4]

Artemisia arborescence plant widely distributed in Saudi Arabia desert and Sinai, Egypt Morocco, Mediterranean region: *Yemen*, and we can found it's in Mediterranean coast, in the Pacific Northwest of the United States, South Africa, parts of Asia and South America.

Artemisia judaica (AJ) is one of the common species of the genus *Artemisia* that grows in Saudi Arabia desert and Sinai, Egypt where animals graze on it. It is widely used in traditional medicine and by Bedouins there. (AJ) has anthelmintic, antibacterial, anti-inflammatory, analgesic and antipyretic effects.^[5,6]

Indeed, the knowledge of herbal medicines were identified by a community, practiced, and heirloomed to the successive generation. Although several synthetic drugs are available to treat various diseases and disorders but, they are not free from side-effects. On the other hand, there is an increasing demand of the herbal medicines as they are safe, effective, economical, eco-friendly and free from deleterious effects. It has been observed that more than sixty percent of the commercially important drugs are obtained from plant sources and a large portion of the world population is dependent on them for their primary healthcare.^[7] Moreover, herbal remedies also provide a cure for certain age-related diseases such as memory loss, immunity related diseases, osteoporosis etc. These days, there are several clinical reports available where natural drugs have shown their promising potential to cure fatal diseases like AIDS, cancer, cardiovascular diseases, and renal disorders. Herbs are a tremendous source of secondary metabolites which protect them against microbes, birds and animals, and attract the plant pollinators too.^[8]

Several secondary metabolites have proved to be very useful for the production of pharmaceutical drugs for human healthcare. Extensive analysis of the phytochemistry of the genus *Artemisia* has led to the identification of various biochemically active secondary metabolites including essential oils, flavonoids, terpenes, esters, and fatty acids. Efficacy trials of these bioactive compounds shall lead to the development of novel herbal drugs for betterment of human health.^[9] *Artemisia* is a widespread genus which encompasses more than 400 species (~474) and is revered as 'Worm wood', 'Mug word', 'Sagebrush' or 'Tarragon'.^[9,10] This genus belongs to the family Asteraceae, sometimes recognized as 'compositae family', 'sunflower family', 'thistle family' or 'daisy family'. The word 'Artemisia' comes from the ancient Greek word: 'Artemis'=The Goddess (the Greek Queen Artemisia) and 'absinthium'=Unenjoyable or without sweetness. The word 'Wormwood' is influenced by the traditional use as a cure for intestinal worms. Most of the *Artemisia* species are perennial, biannual, annual herbaceous ornamental, medicinal and aromatic plant or shrubs. They are silver green, dark green or blue-green in color, possess pungent smell and bitter taste due to presence of terpenoids and sesquiterpene lactones.^[11]

Some species are cultivated as crops while others are used in preparation of tea, tonic, alcoholic beverages and medicines. Apart from non-volatile bioactive compounds, *Artemisia* species are an excellent source of essential oils like thujone, thujyl alcohol, cadinene, phellandrene, pinene etc. which are reported to possess various biological activities including,

antibacterial.^[12] Anti-fungal^[9] anti-viral^[13] anti-malarial^[14] anti-inflammatory^[15] anti-cancer^[16] anti-tumor^[17] anti-helminthic^[13] anti-diabetic^[18-20] anti-spasmodic^[15] hepatoprotective^[21] anti-pyretic^[22] anti-parasitic^[23] anti-oxidant^[16,21,24,25] antifertility^[18] acaricidal^[26] anti-rheumatic^[27] anti-hypertensive^[28,29] trypanocidal, trichomonacidal^[30] wormicidal^[31] emmenagogue, diuretic, abortive^[32] anti-arthritis^[33] immunomodulatory^[34] neuroprotective^[35] menopause, premenstrual syndrome, dysmenorrhea and attention deficit hyperactivity disorder.^[36] Antiulcerogenic^[37] analgesic, bile stimulant^[27] antinociceptive^[38] anti-plasmodial^[39] anti-venom^[40] anti-coccidial^[41] anti-leishmanial^[42,43] anti-hyperlipidemic^[44,45] anti-epileptic and anti-convulsant^[46] anti-cholesterolemic, cholagogue, diuretic, febrifuge and vasodilator^[47] disinfectant^[48], choleric, balsamic, depurative, digestive, emmenagogue, and anti-leukaemia and ant-sclerosis^[49] vermifuges, febrifuge, anti-biotic, urine stimulant^[27] anti-migraine^[50] insecticidal^[51] anti-feedant^[52] abortifacient^[53] anti-herpes virus^[54] and antidote to insect poison.^[55]

Artemisia arborescence (Vaill.) L. It is a woody, aromatic, evergreen shrub, which is used in preparation of folk medicines, flavoring dishes (because of its good aroma) and liqueurs.^[56] It has also been used as an anti-inflammatory agent in traditional medicines. Several other biological activities such as phyto-toxicity.^[57] Anti-bacterial and anti-viral properties^[58,59] have also been reported in the plant extracts. Aqueous extract of aerial parts inhibits the growth of *Listeria monocytogenes* and thus exhibits its anti-bacterial potential.^[56] The plant essential oils also possess antiviral activity against Herpes simplex virus.^[54]

Future Perspectives In recent years, phytochemical investigation of herbal flora has received much attention of the scientists and pharmaceutical industries so as to know about novel herbal compounds which can be screened for their therapeutic potential to treat several health disorders without any side effects. This genus could be a promising source for the development of novel strategies to cure fatal maladies. Undoubtedly, *Artemisia* species possesses a wide range of properties, as evidenced from almost all records of herbal medicine. Because of the dramatic growth in popularity, reliance and extensive demands of pharmaceutical industries.

In this study *artemisia arborescence* freeze -dried extract powder solid dosage form capsules were prepared and analyzed in the pre-formulation study the antitumor activity against breast cancer as herbal supplement product.

MATERIALS AND METHODS

The ethanol extract of *Artemisia Arborescence* concentration was prepared: 100mg/kg. Freeze-dried dried extract of *Artemisia Arborescence*, hard gelatin capsules (Size 0; Color: Red body. Black Cap); Starch, Colloidal Silicon Dioxide (Aerosil), Magnesium Stearate, Sodium Lauryl Sulphate, Microcrystalline Cellulose MCC, Sodium Starch Glycolate SSG, Hydrochloric Acid (0.1NHCl), pH6.8 buffer Solution, and Ethanol. were obtained from Sigma Aldrich. All chemicals used were all of analytical grade and other materials were gift from (Global Pharmaceutical Industry Company-Yemen).

Equipment's: Includes, Oven (Giffin & Geong L-TD) (Metler-Made in Germany); Disintegrator (Erweka- Germany); Dissolution apparatus (SCIENTIFIC Model-DA.60) (Metler- Germany); Balance (Sortorius BP310S NO:91206635- Germany); Balance2 (DENVER Instrument APX-100 - Germany); Hot Plate (Vision Scientific Co. LTD); Freezer (KELON-Model- KDR-20W); Freeze -Dryer (LABONCO Freeze Drier System/LYPH Lock 4.5); Light Microscope; Sieves; Water Bath (CFL 1083 - Germany), UV Spectrophotometer (SHIMADZU Model-UV-1601PC); Capsule filling machine, PH meter (Sartorius PB-11); Chamber 40C" (LAB TECH-LHI-0250E); Chamber 30C" (LAB TECH-LBI-300M).

Determination of The Antitumor Activity of The Extract of *Artemisia Arborescence*

Anticancer activity of *Artemisia arborescence* against breast cancer by using MTT assay against MCF-7. Determine the cytotoxicity of *Artemisia arborescence* against MCF-7 cell line Compared by reference standard evaluation of cytotoxicity of Doxorubicin reference standard against MCF-7 cell line.

Determination of The Organoleptic Properties of The Extract Powder

The following organoleptic properties of *Artemisia Arborescence* materials such as physical appearance, odor and taste were inspected and assessed using the natural senses (e.g. eyes, nose, mouth).

Determination of The Solubility of The Extract Powder

Solubility is an important factor for drug absorption. It is described by the Noyes- Whitney equation: The equilibrium solubility of the freeze -dried extract of *Artemisia arborescence* determined as follows: A saturated solution obtained by stirring excess extract powder solute with distilled water for 3hours at the required temperature (25C°, 37C°) by using water bath until equilibrium has been attained. Samples are withdrawn every 30 minutes and filters.

Absorbance of the sample was measured at (275-296nm for *Artemisia arborescence*) using UV Spectrophotometer. The absorbance reading should increase until one gets to a maximum when equilibrium is reached. This indicates the time required for equilibration.

The solubility was obtained by the following equation:

Solubility = (weight of initial powder - weight of dried residue) / volume of solvent x100%.

Particle Size Determination of The Extract Powder

One of the most fundamental and easy methods for determining particle size is a sieving method. This method involves passing the material being sized through openings of a particular standard size in sieves. So, the degree of fineness of powders is determined by sieving. The sieve receiver and the sieves of number 2.4, 2, 1.6, 0.125, 0.1 were arranged in a descending order on the sieve shaker, then 10g of *Artemisia arborescence* was poured in the top sieve. The process of shaking took 30 minutes. Thereafter the powder collected on each of the sieves was weighed and the percentage(w/w) of each fraction determined.

Determination of The Density of The Extract Powder

A simple test has been developed to evaluate the flowability of a powder by comparing the poured density (bulk density) and tapped density of a powder and the rate at which it packed down. A useful empirical guide is given by Carr's compressibility index equation: ('compressibility' is a misnomer, as compression is not involved).

Carr's index (%) = (Tapped density - Poured density) / Tapped density

In study the density of *Artemisia Arborescence* extract powder was determined as follows: *Artemisia Arborescence* extract powder was poured into the tared cylinder on apparatus up to a volume between 8-10ml before compacting. The cylinder was then weighed and the weight of extract recorded. Thereafter the cylinder was secured in its holder and the reading of unsettled apparent volume, V₀, was taken to the nearest milliliter. The machine was switched on, the powder in the cylinder tapped for approximately 1250 times and the final volume V₁₂₅₀, again taken to the nearest milliliter. The bulk and tapped densities were then calculated using the following equations.

Bulk density (poured density): m / V_0 , in g per ml

Bulk density = weight of the powder / bulk volume

Tapped density: m / V_{1250} , in g per ml.

Tapped density = weight of the powder / tapped volume.

Determination of Flowability of The Extract Powder

The angle of repose ($^{\circ}$) is another important parameter that can be used to describe the flowability of a powder. In the present study a special apparatus was used for the test. The apparatus consisted of a glass cylinder kept in the center of the plate, a plate with scale and a ruler for measuring the height of powder mound. To determine the angle of repose, the glass cylinder was filled with 4 g of plant extract, the cylinder smoothly lifted allowing the powder to flow out at the bottom unto the plate leaving a conical mound. The height and radius of the mound was measured and angle of repose then calculated using the following equation: $\tan \theta = h / r$ θ : Angle of repose, h: height of the conical mound, r: radius of the conical mound.

Determination of The Moisture Content of Extract Powder

About 0.5g of the *Artemisia Arborescence* powdered extract was finely powdered and rapidly weighed in a fiat-bottomed dish. The extract was then dried in an oven at 100- 105°C for 3 hours, allowed to cool (approximately 10 minutes) in a desiccator over anhydrous silica gel, weighed and the weight recorded. The moisture content as determined by this gravimetric method was then calculated using the following equations:

Moisture weight = Initial weight (before drying) - Final weight (after drying), Moisture content = (Moisture weight / Initial weight) 100%.

Formulation of The Extract of *Artemisia Arborescence* Capsules

The selection of the capsule size, the filling machine, the filling method and the excipients where carried out in which 100mg of this drug mixed with excipients as shown in Table 1, place manually in a separate size "0" capsules, then taken four capsules daily to provide the desired dose.

Table 1: Formulation of *Artemisia Arborescence* Capsules.

Ingredient mg / Capsule	Amount/ Unite
Extract	100mg
Starch	45mg
Aerosil	15mg
Microcrystalline Cellulose MCC	116mg
Sodium Starch Glycolate SSG	15mg
Magnesium Stearate	3mg
Sodium Lauryl Sulphate	6mg
Total Weight of Capsules	300mg

Evaluation of The Extract of *Artemisia Arborescence* Capsules^[59-81]**Determination of Uniformity of Weight and The Amount of *Artemisia Arborescence* Capsules**

For the determination of the uniformity of weight, the British Pharmacopoeia method was used. In which Twenty of the *Artemisia arborescence* capsules prepared as described above were taken at random, their contents individually weighed and the average weight (mass) of the content determined. Not more than two of the individual weights (masses) had to deviate from the average weight (mass) by more than 7.5% and none of the deviates by more than twice that percentage. The amount of powder actually filled into the capsules was also compared with the desired quantity and the difference (in percentage) between the desired and actual quantity calculated. According to the formulation, 100mg *Artemisia arborescence* extract was to be filled in one capsule each. Twenty capsules were thus randomly chosen, their contents weighed, the percentage difference between this and the desired weight calculated and averaged for the 20 capsules to assess the accuracy of the filling process.

Determination of Moisture Content of Formulation of *Artemisia Arborescence* Capsules

In this study, the shell of the capsules was removed and the moisture level of the contents of the capsules determined by using the moisture content analyzer.

Determination of The Dissolution Profile of Formulation of *Artemisia Arborescence* Capsules

In this study the basket method was used. Further, the quantitation of the amount of plant material dissolved was measured based on UV absorbance measured at 296 nm, the wavelengths for maximum UV absorption of solutions of the *Artemisia arborescence* extract determined by using a UV- Vis Spectrophotometer.

Determination of Stability of Formulation of *Artemisia Arborescence* Capsules

In which the capsules were stored in a glass bottle container under two conditions by using a climate chamber as shown in Table 2.

Table 2: The Storage Conditions for The Stability Study.

Batch	Temperature °C	Relative humidity (RH)	Container
1	30±2 °C	70%±5% (RH)	Glass Container
2	45±2 °C	70%±5% (RH)	Glass Container

The formulation of *Artemisia arborescence* capsules were stored under the afore-mentioned conditions and every 2 weeks ,6 weeks ,10 weeks and 12 weeks' samples of capsules were taken from each site and assessed for organoleptic properties (i.e. physical nature, color and odor of the powder content and overall size, shape and appearance of the capsule).

At 6 weeks and at the end of 12 weeks the moisture content of the capsules were determined. The organoleptic properties and the moisture level of the content of the test capsules were compared with that of the content of *Artemisia arborescence* capsules before storage.

RESULTS AND DISCUSSION

Evaluation of The Antitumor Activity of *Artemisia Arborescence* Against MCF-7 Cell Line

The results of *Artemisia arborescence* are summarized $IC_{50} = 12.7 \pm 0.48 \mu\text{g/ml}$ strong activity in compare with evaluation of cytotoxicity of Doxorubicin reference standard against MCF-7 cell line $IC_{50} = 0.39 \pm 0.01 \mu\text{g/ml}$.

Yield of Freeze -Dried Extract of *Artemisia Arborescence*

The yields of freeze -dried extract obtained from *Artemisia arborescence* using the method are shown in Table 3, on percentage yield 150 % of extract was obtained from *Artemisia arborescence* crude.

Table 3: Yield of Freeze -Dried Extract of *Artemisia Arborescence*.

Weight of The Dry Powder (g)	Yield of Freeze- Dried Extract	
G	G	%
100	20	150

The Organoleptic Properties of The Freeze -Dried Extract of *Artemisia Arborescence*

As shown in Table 4, the freeze -dried extract and a summary of the organoleptic properties.

Table 4: The Organoleptic Properties of The Extract of *Artemisia Arborescence*.

Properties	<i>Artemisia Arborescence</i>
Physical Appearance	Free-Flowing, Small Particulate Powder
Color	Dark Yellow, Darker than Ground Leave Powder
Odor	Spicy Odor and Characteristic
Taste	Bitter Spicy Taste

The bitter taste and unpleasant odors normally result in poor patient acceptance of dosage forms. Hopefully these negative characteristics still present in the extract can be masked when incorporated in capsule form.

The Solubility of The Freeze -Dried Extract of *Artemisia Arborescence*

For oral solid dosage forms aqueous solubility is a crucial factor influencing the bioavailability of drugs. The results obtained in the solubility testing of the freeze -dried extract of *Artemisia Arborescence* show that the extract is being sparingly soluble in 0.1NHCl.

The Size of Particles of The Freeze -Dried Extract of *Artemisia Arborescence*

Particle size and shape are crucial parameter. They are important for the manufacture of the dosage forms, influence dissolution and bioavailability. Particles can be classified under four different classes as shown in Table 5.

Table 5: British Pharmacopoeia 2013 Appendix XVII A. Particle Size of Powders.

Coarse Powder	Not less than 95% by weight passes through a number 1400 sieve and not more than 40% by weight passes through a number 355sieve.
Moderately Fine Powder	Not less than 95% by weight passes a number 355 sieve and not more than 40% by weight passes through a number 180 sieve.
Fine Powder	Not less than 95% by weight passes a number 180 sieve and not more than 40% by weight passes through a number 125 sieve.
Very Fine Powder	Not less than 95% of the powder by weight passes a number 125 sieve and not more than 40% by weight passes through a number 90 sieve.

Table 6: Particle Size of Freeze -Dried Extract Powders of *Artemisia Arborescence*.

European Sieve No.	ISO Sieve No. (mm)	Wt. Retained
2800	2.5	0
2000	2	0
1400	1.6	0
125	0.125	0.1g
90	0.1	2.2g

The results of the particle size study as shown in Table 6 the *Artemisia arborescence* freeze -dried extract powders were very fine powders based on the British Pharmacopoeia standard.

The Densities of The Freeze - Dried Extract Powders

According to Carr's index % = (Tapp dins. -pour density) / Tapp dins. = 6.82%. The Carr's index of Compressibility for *Artemisia arborescence extract* is 6.82 %. The density study

researches show that the extract of *Artemisia arborescence* freeze -dried extract powders can all be categorized as having excellent flow properties.

The Flowability of The Freeze -Dried Extract Powder

The *Artemisia arborescence* freeze -dried extract powders had angles of repose of 26.9°. Therefore, had good flow properties. This implicated that the *Artemisia arborescence* freeze -dried extract powders possessed appropriate excellent flowability for the manufacture of capsule dosage form as shown in Table 7.

The Moisture Content of The Extract

Table 7: Pre-Formulation Testing Results of *Artemisia Arborescence*.

Testing	<i>Artemisia Arborescence</i>
The Solubility of Extract	Sparingly Soluble
Particle Size	Very Fine Powder
Carr's Index (%)	6.82%
Angle of Repose (°)	26.9°
The Moisture Content (%)	3.11%

The results of moisture content were 3.11%. The total dose divided into small doses. Which will be suitable to be filled in capsule, the chosen capsule size was (0) and we will need for 4 capsule each one will be contain 100mg of *Artemisia arborescence* freeze dried.

Moisture Level of The Content of *Artemisia Arborescence* Capsules

After the capsules were filled the moisture level of its contents were again tested just to ascertain if there had been changes in moisture level during the manufacturing procedure. The results of these tests are given and indicated that the moisture level of the contents of the *Artemisia arborescence* capsules were 6 % and When analyzed in the pre-formulation study, the moisture content for the *Artemisia arborescence* extract were however 3.11%. Thus, appeared to have a slight increase in the moisture level of the *Artemisia arborescence* material after encapsulation. This suggested that this extract absorbed some moisture during the filling procedure, presumably because it was hygroscopic.

The Dissolution Profile of *Artemisia Arborescence* Capsules

The results of the dissolution studies on the *Artemisia arborescence* capsules as shown in Table 8 showed that >60% of the *Artemisia arborescence* capsule contents dissolved in the dissolution medium within 45 minutes.

Table 8: The Dissolution Rate of Formulation of *Artemisia Arborescence* Capsules.

Time (min)	%Amount Dissolve			
	F1	F2	F3	F4
5	13.48	14	22.47	7.33
15	43.45	44.83	37.67	46.67
30	51.84	59.30	44.13	89.44
45	57.89	68.20	52.50	96.60
60	60.34	74.13	73.50	99.90

Stability of Formulation *Artemisia Arborescence* Capsules

For the study of Stability, two batches of capsules were stored under the different conditions. And the results of the organoleptic properties, moisture content tested during stability study.

The Organoleptic Properties of Formulation *Artemisia Arborescence* Capsules

When *Artemisia arborescence* capsules were stored in the glass container, whether at $30\pm 2^{\circ}\text{C}$ / $70\%\pm 5\%$ RH and $45\pm 2^{\circ}\text{C}$ / $75\%\pm 5\%$ RH, the organoleptic properties of the plant material remained relatively unchanged during the 12 weeks' storage the results were shown in Table 9.

Table 9: Organoleptic Properties of *Artemisia Arborescence* Capsules Stored.

No Week	Size, Shape of Capsule	Gross Nature of Powder in Capsule	Color of Powder	Odor of Powder
0	Regular 'O' Size & Shape	Powder	Brown	No Change
2	No Change	Powder	Brown	No Change
6	No Change	Powder	Brown	No Change
10	No Change	Powder	Brown	No Change
12	No Change	Powder	Brown	No Change

The Moisture Content of Formulation *Artemisia Arborescence* Capsules

The moisture levels of the *Artemisia arborescence* capsules contents at 6 weeks and at the end of 12 weeks were shown in Table 10. The results were compared with that of the content of *Artemisia arborescence* capsules before storage.

Table 10: The Moisture Levels of Formulation of *Artemisia Arborescence* Capsules.

Time	Percentage of Moisture%
Before Storage	3.11%
After 6 weeks at $30\pm 2^{\circ}\text{C}$ / $70\%\pm 5\%$ (RH)	3%
After 6 weeks at $45\pm 2^{\circ}\text{C}$ / $75\%\pm 5\%$ (RH)	3%
After 12 weeks at $30\pm 2^{\circ}\text{C}$ / $70\%\pm 5\%$ (RH)	3.3%
After 12 weeks at $45\pm 2^{\circ}\text{C}$ / $75\%\pm 5\%$ (RH)	3.4%

From the results as shown in Table 10, there was no large change in the moisture levels of the *Artemisia arborescence* capsules stored in the glass bottle containers under high temperature $45\pm 2^{\circ}\text{C}$ / $75\%\pm 5\%$ (RH) and $30\pm 2^{\circ}\text{C}$ / $70\%\pm 5\%$ (RH) during storage, and it is strongly suggested that storage in glass bottle containers protect *Artemisia arborescence* capsules against moisture.

CONCLUSION

Freeze -dried extract powders of *Artemisia arborescence* have good flowability, regular particle size and shape, is soluble with high wettability, on average contained 3.11 % moisture for *Artemisia arborescence*. Elegant capsules that were uniform in content and weight, respectively, Moreover, the manufactured capsules and release solid oral dosage forms and had good bioavailability. The results showed that the extract *Artemisia arborescence* was suitable as raw materials of the plants as far as manufacture of capsules were concerned, but that the stability of these extract containing capsules was acceptable. The antitumor activity of ethanol extract of *Artemisia arborescence* was evaluated at the dose of 100mg/kg and showed a significant activity. The best formulation F4 according to dissolution was 96.6% after 45 min, and stability under various storage condition were evaluated.

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REFERENCES

1. WHO, Guidelines for the Assessment of Herbal Medicines. In WHO Expert Committee on Specifications for Pharmaceutical Preparations, Geneva, Switzerland., 1999; 6a(34): 178 - 184.
2. GNDP (Ghana National Drug Programme), A Manual of Harmonized Procedures for Assessing the Safety, Efficacy and Quality of Plant-Medicines in Ghana, Ministry of Health, Ghana., 2004.
3. Richter M. Discussion Paper Prepared for The Treatment Action Campaign and AIDS Law Project., 2003; 7.
4. Dennis VC, Awang Tyler's. Herbs of Choice, The Therapeutic Use of Phytomedicinals. 3rd Edition, CRC Press, Tylor and Francis Group, NewYork., Chapter 1 p.1-17 & Chapter 4. 2009; 72.

5. RHS Plant Selector - *Artemisia Arborescence* 'Powis Castle'. Retrieved 2 June. RHS A-Z encyclopedia of garden plants. United Kingdom: Dorling Kindersley., 2008; 1136.
6. Cubukcu B, Bray DH, Warhurst DC, Mericli AH, Ozhatay N, et al. In vitro Antimalarial Activity of Crude extracts and compounds from *Artemisia abrotanum* L. *Phytother Res.*, 1990; 4: 203-204.
7. Kennedy DO, Wightman EL. Herbal Extracts and Phytochemicals Plant Secondary Metabolites and the Enhancement of Human Brain Function. *Adv Nutr.*, 2011; 2: 32-50.
8. Obistioiu D, Cristina RT, Schmerold I, Chizzola R, Stolze K, et al. Chemical Characterization by GC–MS and In-vitro Activity Against *Candida Albicans* of Volatile Fractions Prepared from *Artemisia Dracunculus*, *Artemisia Abrotanum*, *Artemisia Absinthium* and *Artemisia Vulgaris*. *Chem Cent J.*, 2014; 8: 1-11.
9. Tajadod G, Mazooji A, Salimpour F, Samadi N, Taheri P. The Essential Oil Composition of *Artemisia Vulgaris* L. in Iran. *Ann Biol Res.*, 2012; 3: 385-389.
10. Abad MJ, Bedoya LM, Apaza L, Bermejo P. The *Artemisia* L. Genus: a Review of Bioactive Essential Oils. *Molecules.*, 2012; 17: 2542-2566.
11. Altunkaya A, Yildirim B, Ekici K, Terzioglu O. Determining Essential Oil Composition, Antibacterial and Antioxidant Activity of Water Wormwood Extracts. *GIDA.*, 2014; 39: 17-24.
12. Rajeshkumar PP, Hosagoudar VB. Mycorrhizal Fungi of *Artemisia Japonica*. *Bulletin Basic Applied Plant Biol.*, 2012; 2: 7-10.
13. Mojarreb M, Emami SA, Gheibi S, Taleb AM, Afshar FH. Evaluation of Antimalarial Activity of *Artemisia Turcomanica* and *A. Kopetdagensis* by Cellfree β -hematin Formation Assay., *Res J Pharmacognosy.*, 2016; 3: 59-65.
14. Taherkhani M. *In-Vitro* Cytotoxic Activity of The Essential Oil Extracted from *Artemisia Absinthium*. *Iran J Toxi.*, 2014; 8: 1152-1156.
15. Shafi G, Hasan TN, Syed NA, Al-Hazzani AA, Alshatwi AA et al. *Artemisia Absinthium* (AA) a Novel Potential Complementary and Alternative Medicine for Breast Cancer. *Mol Biol Rep.*, 2012; 39: 7373-7379.
16. Ashok PK, Upadhyaya K. Preliminary Phytochemical 511 Screening and Physico–Chemical Parameters of *Artemisia Absinthium* and *Artemisia Annua*. *J Pharmacogn Phytochem.*, 2013; 1: 229-235.
17. Nathar VN, Yatoo GM. Micropropagation of an Antidiabetic Medicinal Plant, *Artemisia Pallens*. *Turk J Bot.*, 2014; 38: 491-498.

18. Joshi RK, Satyal P, Setzer WN. Himalayan Aromatic Medicinal Plants: A Review of their Ethnopharmacology, Volatile Phytochemistry, and Biological Activities., Medicines., 2016; 3: 6.
19. Mohammadian A, Moradkhani S, Ataei S, Shayesteh TH, Sedaghat M et al. Antioxidative and Hepatoprotective Effects of Hydroalcoholic Extract of Artemisia Absinthium L. in rat. J Herb Med Pharmacol., 2016; 5: 29-32.
20. Hailu T, Beraand BA, Mariam EG. *In-vitro* Mass Propagation of Artemisia (Artemisia Annu L.) cv: Anamed. Plant Tissue Cult & Biotech., 2013; 23: 165-176.
21. Yildiz K, Basalan M, Duru O, Gokpinar S. Antiparasitic Efficiency of Artemisia Absinthium on Toxocara Cati in Naturally Infected Cats. Turkiye Parazitoloji Dergisi., 2011; 35:10-14.
22. Bora KS, Sharma A. Evaluation of Antioxidant and Free-Radical Scavenging Potential of Artemisia Absinthium. Pharm Biol., 2011; 49: 1216-1223.
23. Msaada K, Salem N, Bachrouch O, Bousselmi S, Tammar S et al. Chemical Composition and Antioxidant and Antimicrobial Activities of Wormwood (Artemisia Absinthium L.) Essential Oils and Phenolics. J Chem., 2015; 1-12.
24. Godara R, Parveen S, Katoch R, Yadav A, Verma PK et al. Acaricidal Activity of Extract of Artemisia Absinthium Against Rhipicephalussanguineus of Dogs. Parasitol Res., 2014; 113: 747-754.
25. Saxena RBV. Entirely Gone Out Useful Plant-Artemisia Cina. Indo American J Pharmaceutical Sci., 2015; 2: 648-663.
26. Tigno XT, de Guzman F, Flora AM. Phytochemical Analysis and Hemodynamic Actions of Artemisia Vulgaris L. Clin Hemorheol Microcirc., 2000; 23: 167-175.
27. Sharopov FS, Sulaimonova VA, Setze WN. Composition of The Essential Oil of Artemisia Absinthium from Tajikistan. Rec Nat Prod., 2012; 6: 127-134.
28. Nibret E, Wink M. Volatile Components of Four Ethiopian Artemisia Species Extracts and Their *In-vitro* Anti-Trypanosomal and Cytotoxic Activity. Phytomedicine., 2010; 17: 369-374.
29. Bizhani N. Herbal Therapy and Treatment of Worm Infections, Emphasizing Taenia Solium. Iran J Public Health., 2015; 44: 1555-1556.
30. Kader JC, Delseny M. Advances in Botanical Research. Academic Press., 2011; 60.
31. Kim WS, Choi WJ, Lee S, Kim WJ, Lee DC et al. Anti-inflammatory, Antioxidant and Antimicrobial Effects of Artemisinin Extracts from Artemisia Annu L. Korean. J Physiol Pharmacol., 2015; 19: 21-27.

32. Zamanai TRS, Iranshahi M, Rastin M, Tabasi N, Mahmoudi M. *In-vitro* Immunomodulatory Properties of a Sesquiterpene Lactone-Bearing Fraction from *Artemisia Khorassanica*. *J Immunotoxicol.*, 2015; 12: 223-230.
33. Lachenmeier DW. Wormwood (*Artemisia Absinthium* L.)-a Curious Plant with Both Neurotoxic and Neuroprotective Properties. *J Ethnopharmacol.*, 2010; 131: 224-227.
34. Adams JC, Garcia C, Garg G. Mugwort (*Artemisia Vulgaris*, *Artemisia Douglasiana*, *Artemisia Argyi*) in The Treatment of Menopause, Premenstrual Syndrome, Dysmenorrhea and Attention Deficit Hyperactivity Disorder. *Chin Medi.*, 2012; 3: 116-123.
35. Jaleel GARA, Abdallah HMI, Gomaa NES. Pharmacological Effects of Ethanol Extract of Egyptian *Artemisia Herba-alba* in Rats and Mice. *Asian Pac J Trop Biomed.*, 2016; 6: 44-49.
36. Shoaib M, Shah I, Ali N, Shah WA. A Mechanistic Approach to Anti-nociceptive Potential of *Artemisia Macrocephala* Jacquem. *BMC Complement Altern Med.*, 2016; 16: 141.
37. Ramazani A, Sardari S, Zakeri S, Vaziri B. *In-vitro* Antiplasmodial and Phytochemical Study of Five *Artemisia* Species from Iran and *In-vivo* Activity of Two Species. *Parasitol Res.*, 2010; 107: 593-599.
38. Nalbantsoy A, Erel SB, Koksall C, Gocmen B, Yildiz MZ et al. Viper Venom Induced Inflammation with *Montivipera Xanthina* and the anti-snake Venom Activities of *Artemisia Absinthium* L. in Rat. *Toxicon.*, 2013; 65: 3440.
39. Kostadinovic L, Levic J, Galonja-Coghill T, Ruzicic L. Anticoccidial Effects of the *Artemisia Absinthium* L. Extracts in Broiler Chickens. *Archiva Zootechnica.*, 2012; 15: 69-77.
40. Tariku Y, Hymete A, Hailu A, Rohloff J. Essential Oil Composition, Antileishmanial and Toxicity Study of *Artemisia Abyssinica* and *Satureja Punctata* ssp. *Punctata* from Ethiopia *Chem Biodivers.*, 2010; 7: 1009-1018.
41. Jafroodi K, Farazmand A, Amin M, Doroodgar A, Shirzadi MR et al. Methanolic Extract's Activity of *Artemisia Absinthium*, *Vitexagnus-Castus* and *Phytolacaamericana* Against *Leishmania Major* *In-vitro* and *In-vivo*. *Int Arch Health Sci.*, 2015; 2: 69-74.
42. Daradka HM, Badawneh M, Al-jamal JA, Bataineh Y. Hypolipidemic Efficacy of *Artemisia Absinthium* Extracts in Rabbits. *World Appl Sci J.*, 2014; 31: 1415-1421.
43. Khan KA. A Preclinical Antihyperlipidemic Evaluation of *Artemisia Vulgaris* Root in Diet Induced Hyperlipidemic Animal Model. *Int J Pharm Res* 2015; 5: 110-114.

44. De Almeida ER, da Silva AR, Aragatilde AC, dos Santos Soares PH et al. Anticonvulsant and Anxiolytic Assessment of Leaves from *Artemisia Vulgaris* L. in Mice. *J Med Plant Res.*, 2013; 7: 3325-3331.
45. Sajid M, Khan MR, Shah NA, Ullah S, Younis T et al. Proficiencies of *Artemisia Scoparia* Against CCl₄ Induced DNA Damages and Renal Toxicity in Rat. *BMC Complement Altern Med.*, 2016; 16: 149.
46. Nikhat S, Ahmad S, Akhtar J, Jamil S. Phytochemical and ethnopharmacological perspective of Afsantin (*Artemisia Absinthium* Linn.). *Anna Phytomed.*, 2013., 2: 105-109.
47. Ali M, Abbasi BH. Thidiazuron–Induced Changes in Biomass Parameters, Total Phenolic Content and Antioxidant Activity in Callus Cultures of *Artemisia Absinthium* L. *Appl Biochem Biotechnol.*, 2014; 172: 2363-2376.
48. Gohari AR, Kurepaz-Mahmoodabadi M, Saeidnia S. Volatile Oil of *Artemisia Santolina* Decreased Morphine Withdrawal Jumping in Mice. *Pharmacognosy Res.*, 2013; 5: 118-120.
49. Bouzenna H, Krichen L, Pelargonium Graveolens L'Her. *Artemisia Arborescens* L. Essential Oils: Chemical Composition, Antifungal Activity Against *Rhizoctonia Solani* and Insecticidal Activity Against *Rhyssopertha Dominica*. *Nat Prod Res.*, 2012; 27: 841-846.
50. Barrero AF, del Pino MMH, Portero AG, Burón PA, Arteaga JF et al. Terpenes and Polyacetylenes from Cultivated *Artemisia Granatensis* Boiss (Royal chamomile) and Their Defensive Properties. *Phytochemistry.*, 2013; 94: 192-197.
51. Zadoks JC. Crop Protection in Medieval Agriculture: Studies in Premodern Organic Agriculture. Sidestone Press., 2013.
52. Gavanji S, Sayedipour SS, Larki B, Bakhtari A. Antiviral Activity of some Plant Oils Against Herpes Simplex Virus Type 1 in Vero Cell Culture. *J Acute Med.*, 2015; 5: 62-68.
53. McKenna DJ, Hughe K. The Incense Bible: Plant Scents That Transcend World Culture, Medicine, and Spirituality. Routledge., 2014.
54. Brown GD. The Biosynthesis of Artemisinin (Qinghaosu) and The Phytochemistry of *Artemisia Annu* L. (Qinghao). *Molecules.*, 2010; 15: 7603-7698.
55. Militello M, Settanni L, Aleo A, Mammina C, Moschetti G et al. Chemical Composition and Antibacterial Potential of *Artemisia Arborescens* L. Essential Oil. *Curr Microbiol.*, 2011; 62: 1274-1281.

56. Araniti F, Lupinia A, Sorgonà A, Conforti F, Marrelli M et al. Allelopathic Potential of *Artemisia Arborescens*: Isolation, Identification and Quantification of Phytotoxic Compounds Through Fractionation-guided Bioassays. *Nat Prod Res.*, 2013; 27: 880-887.
57. Erel SB, Reznicek G, Senol SG, Yavasoglu NUK, Konyalioglu S et al. Antimicrobial and Antioxidant Properties of *Artemisia L.* Species from Western Anatolia. *Turk. J Biol.*, 2012; 36: 75-84.
58. Younes K, Merghache S, Djabou N, Merghache D, Muselli A et al. Chemical Composition, Antibacterial and Antioxidant Activities of New Essential Oil Chemotype of Algerian *Artemisia 1068 Arborescens L.* *Afr J Pharm Pharmacol.*, 2012; 6:2912- 2921.
59. *International Journal of Pharmaceutics.*, 2006; 321: 1–11.
60. Saif AA, Alburyhi MM, Noman MA. Evaluation of Vitamin and Mineral Tablets and Capsules in Yemen Market. *Journal of Chemical Pharma Research.*, 2013; 5(9):15-26.
61. Wells J. *Pharmaceutics The Science of Dosage Form Design.* 2nd ed. Edited by M. E. Aulton, Churchill Livingstone., 2002; 114, 129, 130, 134.
62. Paget GE, Barnes JM. Toxicity Tests. In: Laurence DR, Bacharach AL (ed.) *Evaluation of Drug Activities. Pharmacometrics.* London: Academic Press., 1964; 161.
63. Turkoglu M, Sakr A. Tablet Dosage Forms. In: Florence AT, Siepmann J. eds. *Modern Pharmaceutics*, New York: Informa Healthcare., 2004; 1: 281–222.
64. Alburyhi MM, El-Shaibany A. Formulation and Evaluation of Anti-peptic Ulcer Capsules of *Curcuma Longa* Herbal Product. *World Journal of Pharmaceutical Research.*, 2023; 12(22): 76-96.
65. Komperlla, MK. The Formulation and Evaluation on of Rapid Release Tablets Manufactured from *Artemisia Afra* Plant Material. A Thesis. A Master's Thesis. University of the Western Cape., 2004.
66. Alburyhi MM, Saif AA, Noman MA, Saeed SA, Al-Ghorafi MA. Formulation and Evaluation of Diclofenac Orodispersible Tablets. *European Journal of Pharmaceutical and Medical Research.*, 2023; 10(9): 01-06.
67. Aboghanem A, Alburyhi MM, Noman MA. Effect of Different Excipients on Formulation of Immediate Release Artemether/Lumefantrine Tablets. *Journal of Chemical Pharm Research.*, 2013; 5(11):617-625.
68. Alburyhi MM, Saif AA, Noman MA, Yahya TA. Formulation, Development and Evaluation of Famotidine Orodispersible Tablets. *European Journal of Pharmaceutical and Medical Research.*, 2023; 10(10): 56-62.

69. Saif AA, Alburyhi MM, Noman MA, Almaktari AM. Formulation and Evaluation of Trimetazidine Hydrochloride and Clopidogrel Bisulphate Multi-unit Solid Dosage Forms. *Journal of Chemical Pharm Research.*, 2014; 6(2):421-426.
70. Alburyhi MM, Saif AA, Noman MA, Al khawlani MA. Formulation and Evaluation of Bisoprolol Fast Dissolving. *World Journal of Pharmaceutical Research.*, 2023;12(16):01-10.
71. Bary AA, El-Gazayerly ON, Alburyhi MM. Formulation of Immediate Release Lamotrigine Tablets and Bioequivalence Study. *Journal of Chemical Pharm Research.*, 2013; 5(10):266–271.
72. Alburyhi MM, El-Shaibany A. Formulation and Evaluation of Effervescent Granules of *Artemisia Arborescence* Herbal Product for Foodborne Illness. *World Journal of Pharmacy and Pharmaceutical Sciences.*, 2023; 12(12): 1429-1444.
73. Alburyhi MM, Saif AA, Noman MA, Yahya TA, Al-Ghorafi MA. Formulation and Evaluation of Drotaverine Orally Disintegrating Tablets. *World Journal of Pharmaceutical Research.*, 2023; 12(18): 66-79.
74. Saif AA, Alburyhi MM, Noman MA. Formulation and Evaluation of Ketoprofen Fast Dissolving Tablets. *International Journal of Sciences.*, 2018;7(09):27- 39.
75. Alburyhi MM, Saif AA, Noman MA, Salim YA, Hamidaddin MA. Formulation and Evaluation of Lisinopril Orally Disintegrating Tablets. *World Journal of Pharmacy and Pharmaceutical Sciences.*, 2023; 12(9): 357-369.
76. Hamidaddin MA, Alburyhi MM, Noman MA, Saif AA. Formulation and Evaluation of Rosuvastatin Fast Dissolving Tablets. *World Journal of Pharmacy and Pharmaceutical Sciences.*, 2023; 12(9): 2293-2303.
77. Alburyhi MM, Saif AA, Noman MA, Saif RM. Recent Innovations of Delivery Systems for Antimicrobial Susceptibility Study of Ciprofloxacin Biodegradable Formulations for Post-Operative Infection Prophylaxis. *European Journal of Pharmaceutical and Medical Research.*, 2023; 10(9), 32-36.
78. Alburyhi MM, Saif AA, Noman MA, Saif RM. Recent Innovations of Delivery Systems for Antimicrobial Susceptibility Study of Ceftriaxone Biodegradable Formulations for Post-Operative Infection Prophylaxis. *European Journal of Pharmaceutical and Medical Research.*, 2023; 10(8), 95-99.
79. Alburyhi MM, Saif AA, Noman MA. Stability Study of Six Brands of Amoxicillin Trihydrate and Clavulanic Acid Oral Suspension Present in Yemen Markets. *Journal of Chemical Pharm Research.*, 2013; 5(5):293-296.

80. Alburyhi MM, El-Shaibany A. Formulation and Evaluation of Oral Pharmaceutical Solution of Pandanus Odoratissimus L Extract Herbal Product in Treatment of Nocturnal Enuresis. World Journal of Pharmacy and Pharmaceutical Sciences., 2024; 13(1): 1840-1851.
81. World Health Organization Quality Control Methods for Medicinal Plant Materials. World Health Organization Geneva., 1998.