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FORMULATION AND EVALUATION OF ANTIBACTERIAL ORODISPERSIBLE TABLETS OF ARTEMISIA ARBORESCENE EXTRACT HERBAL PRODUCT

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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 repellant, as flavorings 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 cytotoxic activity of Artemisia arborescence can be attributed to the presence of α-bisabolol and palmitic acid. The extract has high the antibacterial and antiviral activity. *Artemisia arborescence* is commonly used in traditional medicine for a wide range of ailments including gastritis, gastric ulcer and food poisoning. Antibacterial activity of ethanol extract of Artemisia arborescence was evaluated at the dose of 250mg/kg and showed a significant activity. *Artemisia arborescence was f*ormulated as Orodispersible tablets ODTs and evaluate for organoleptic properties of ethanol extract of *Artemisia arborescence*. The results show that the extract was sparingly soluble, excellent flowability of extract powder, the best formulation of Orodispersible tablets, ODTs is F4 the release rate was 95.51% after 5min and disintegration time within 4min.

KEYWORDS: *Artemisia arborescence*, Extract, Orodispersible tablets, ODTs, Herbal Products.

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 'composite 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-coccidal,[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] choleretic, 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 the present study, Orodispersible tablets ODTs of *Artemisia arborescence* are planned to prepare with an intention to improve disintegration, dissolution rate and bioavailability of the drug. The Orodispersible tablets ODTs will be prepared by direct compression method are evaluated for various quality control tests for tablets such as hardness, friability, weight variation, drug content uniformity, disintegration and dissolution. Fast dissolving tablets will also help in ease of administration because fast dissolving tablets give uniform dispersion product.

This study *Artemisia arborescence freeze* -dried extract Orodispersible tablets ODTs solid dosage forms was prepared and analyzed in the pre-formulation study the total assessments were performed in the pre-formulation study. *Artemisia arborescence* possess the antibacterial and antiviral activity.

MATERIALS AND METHODS

The powder ethanol extract of *Artemisia arborescence* with the following concentration were prepared: 250mg/kg dried extract of *Artemisia Arborescence*, Orodispersible tablets ODTs: Lactose, Starch, Microcrystalline Cellulose, Carboxyl Methylcellulose, Colloidal Silicon Dioxide (Aerosil), Croscarmellose Sodium, Sodium Starch Glycolate, Na Lauryl Sulfate, Magnesium Stearate, Aspartame, Peppermint Flavor, were gift from (Global Pharmaceutical Industry Company-Yemen). Hydrochloric acid (HCl), 6.8pH Buffer Solution, and Ethanol were obtained from Sigma Aldrich. All chemicals used were all of analytical grade.

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); Sieving Granulator, Tablet compression machine, Hardness tester, Friability Test Apparatus, Powder mixer , DSC, PH meter (Sartorius PB-11); Chamber 40C" (LAB TECH-LHI-0250E); Chamber 30C" (LAB TECH-LBI-300M).

Determination of The Organoleptic Properties of the Extract Powder

The following organoleptic properties of *Artemisia arborescence* extract such as physical appearance, odor and taste were inspected and assessed using the natural senses (e.g. eyes, nose, mouth). determine the moisture content, pH and melting point of fine powder.

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 (25°C, 37°C) by using water bath until equilibrium has been attained. Samples are withdrawn every 30 minutes and filters. Absorbance of the sample was measured at (275-296 nm 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%.

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 taped 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 /V0, in g per ml

Bulk density = weight of the powder / bulk volume

Tapped density: m /V1250, in g per ml.

Tapped density = weight of the powder / tapped volume

Determination of Flowability of The Extract Powder

The angle of repose (0) is another important parameter that can be used to describe the flowability of a powder (Wells, 2002). 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.

Formulation of The Extract of *Artemisia Arborescence* Orodispersible Tablets ODTs

The selection of Orodispersible tablets ODTs, the tablet press machine, the filling method and the excipients where carried out in which 250mg of this extract mixed with excipients as shown in Table 1**,** place manually in a equal size then taken Orodispersible tablets ODTs daily to provide the desired dose.

Table 1: Formulation Batches of *Artemisia Arborescence* Orodispersible Tablets ODTs.

Formulations (mg)	Quantity Per Tablet (mg)						
	F1	F2	F3	F4	F5	F6	F7
Extract	250	250	250	250	250	250	250
Lactose	___	___	___	322.5	190	190	___
Starch	322.5	___	132.5	___	132.5	___	___
Microcrystalline Cellulose (MCC)	145	167	117.5	117.5	167.5	117.5	467.5
CMC	___	323	190	___	___	132.5	___
Aerosil	112.5	112.5	112.5	112.5	112.5	112.5	112.5
Sodium Starch Glycolate (SSG)	150	100	50	___	___	100	150
Croscarmellose Sodium	___	___	100	150	100	50	___
Mg. Stearate	___	2.5	2.5	2.5	2.5	2.5	___
Na Lauryl Sulfate	___	25	25	25	25	25	___
Aspartame	10	10	10	10	10	10	10
Peppermint Flavor	10	10	10	10	10	10	10

Orodispersible tablets ODTs were prepared by direct compression method all the ingredients were passed through 60 mesh sieves separately. Then drug and diluents separately taking small portion of both each time and blending it thoroughly to get uniform mixture. The mixture was compressed using 17* 9 mm size to get a tablet of 1000mg weight using mini tablet press machine.

Evaluation of The Extract of *Artemisia Arborescence* Orodispersible Tablets ODTs[60-82]

Determination of the Weight Variation of *Artemisia Arborescence* Orodispersible Tablets ODTs

Twenty tablets were taken and their weights were determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight. Average weight was compared with the individual weight and the percentage deviation of individual tablet was calculated.

Determination of The Hardness of *Artemisia Arborescence* Orodispersible Tablets ODTs

Twenty tablets were taken and their Hardness was determined by taking tablets from each formulation and was measured by using hardness tester. The hardness was measured in terms of kg/cm^3.

Determination of The Friability of *Artemisia Arborescence* Orodispersible Tablets ODTs

Twenty tablets were taken and their friability of the tablet was measured using an friabiliator. Twenty reweighed tablets were rotated at 25 rpm for 4 rpm and dropping the tablets at a height of 6 inches at each revolution and the tablets were subjected to 100 Revolutions. The tablets were then deducted and reweighed and the percentage of weight loss was calculated. The percentage friability of the tablets were measured as per the following formula. Percentage friability = (Initial weight – final weight/ Initial weight) ×100.

Determination of The Disintegration Time of *Artemisia Arborescence* Orodispersible Tablets ODTs

Disintegration time was measured using disintegration test apparatus. A tablet was placed in each six tube of the basket. The basket with the bottom surface is made up of stainless – steel screen was immersed in water maintained at 37°C as the disintegration fluid and the paddle at 100rpm as stirring element was used. The time taken for complete disintegration of the tablet with no palatable mass remaining in the apparatus was measured in seconds.

Determination of The Dissolution Profile of *Artemisia Arborescence* Orodispersible Tablets ODTs

In this study the paddle method was used. Further, the quantitation of the amount of plant material dissolved was measured based on UV absorbance measured at 296nm the wavelengths for maximum UV absorption of solutions of the *Artemisia arborescence* extract determined by using a UV- Vis Spectrophotometer. The fast dissolving tablets FDTs were placed inside the dissolution vessel. The dissolution apparatus used for this study was USP Type-II apparatus of which paddle was set at a speed of 75rpm Samples of 5ml were withdrawn at time intervals 5, 10, 20, 30, 45 and 60 min. The volume of dissolution fluid is adjusted to 900 ml by replacing 5 ml of fresh dissolution medium after each sampling and thus sink condition was maintained. In this study the dissolution medium used was 0.1N HCl and temperature of 37 ± 0 .5°C was maintained throughout the dissolution studies. Each sample was diluted to 10 ml and analyzed at 296 nm using double beam UV and visible Spectrophotometer against reagent blank.

RESULTS AND DISCUSSION

Evaluation of *Artemisia Arborescence* Orodispersible Tablets ODTs

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

The 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 fine powder acidic pH 4.30, moisture content 3.11% and melting point of fine powder (MP) 121°C. The best solubility in ethanol and acidic medium soluble 0.1N HCl.

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

As shown in Table 2 the freeze -dried extract and a summary of the organoleptic properties.

Table 2: The Organoleptic Properties of Extract of *Artemisia Arborescence.*

Properties	*Artemisia Arborescence*
Physical Appearance	Free-flowing, small particulate powder, which clumps together to form a solid mass on prolong exposure to air.
Color	Light Brown, changing to dark brown on prolong exposure to air.
Odor	Characteristic odour, odour still present after 15 mins on watch glass.
Taste	Bitter (extremely)

The Densities of The Freeze - Dried Extract

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

The *Artemisia arborescence* freeze -dried extract powders had angles of repose of 26.9°. Therefore, had excellent flow properties. This implicated that the *Artemisia arborescence* freeze -dried extract powders possessed appropriate excellent flowability for the manufacture of Orodispersible tablets ODTs dosage form as shown in Table 3.

Table 3: Pre-formulation Testing Results on *Artemisia Arborescence*.

Testing	*Artemisia Arborescence*
The Solubility of Extract	sparingly Soluble
Particle Size	Very Fine Powder
Carr's Index (%)	6.82%
Angle of Repose (°)	26.9°

The total dose divided into small doses. Which will be suitable to be compressed to tablets, the chosen tablet and we will need for 4 tablets each one will be contain 250mg of *Artemisia arborescence* freeze dried Orodispersible tablets ODTs.

Weight Variation of *Artemisia Arborescence* Orodispersible Tablets ODTs

The weight variation in all the ten formulation was found to be 1000±8.779mg. Formulations were within pharmacopoeia limits with free flow of the powder blend and demonstrating the efficiency of compression of particles into tablets.

Hardness of *Artemisia Arborescence* Orodispersible Tablets ODTs

The hardness was maintained to be within 4.16±0.25kg/cm^2 as these tablets are rapidly disintegrating. No variation in the hardness was found which clearly indicates that the proper blending of the mixture for the preparation of Orodispersible tablets. The prepared tablets in all the formulation possess good mechanical strength with sufficient hardness.

Friability of *Artemisia Arborescence* Orodispersible Tablets ODTs

Percentage friability is below 1% it is 0.049%, it indicated that of good mechanical resistance of the tablets.

Disintegration of *Artemisia Arborescence* Orodispersible Tablets ODTs

The results of the disintegration studies on the *Artemisia arborescence* Orodispersible tablets ODTs are shown in Table 4.

Table 4: Disintegration of *Artemisia Arborescence* Orodispersible Tablets ODTs.

Formulations	F1	F2	F3	F4	F5	F6	F7
Disintegration Time(min)	2.9	>45	>45	4	2.8	>45	1.2

Dissolution profile of *Artemisia arborescence* Orodispersible Tablets ODTs

The results of the dissolution studies on the *Artemisia arborescence* Orodispersible tablets ODTs are shown in Table 5 showed that >95% of the *Artemisia arborescence* Orodispersible tablets ODTs contents dissolved in the dissolution medium within 5 minutes.

Table 5: The Dissolution Rate of *Artemisia Arborescence* Orodispersible Tablets ODTs.

Time(min)	% Dissolution			
	F1	F4	F5	F7
5	76.39	95.51	85.86	76.39
10	86.51	88.88	84.46	77.83
20	76.74	86.71	83.36	99.90
30	71.74	85.28	81.04	100.00
45	69.13	84.85	70.70	83.23
60	68.04	76.02	69.12	82.16

CONCLUSION

Freeze -dried extract powder of *Artemisia arborescence* has good flowability, regular particle size and shape, is soluble with high wetability, on average contained 3.11 % moisture for *Artemisia arborescence*. Elegant Orodispersible tablets ODTs that were uniform in content and weight variation, friability, respectively, moreover, the manufactured Orodispersible tablets ODTs and release solid oral dosage forms except some formulations not conform in disintegration time. Orodispersible tablets ODTs is prepared by direct compression method and our study showed that the best formulation of Orodispersible tablets ODTs is F4 according to dissolution was 95.51%after 5 min, and stability under various storage condition were evaluated.

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