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FORMULATION, DEVELOPMENT AND EVALUATION OF *CHAMOMILE* EXTRACT CAPSULES DELIVERY SYSTEM AS AN ADVANCED PHYTOTHERAPY APPROACH FOR GOUT

Prof. Dr. Mahmoud Mahyoob Alburyhi[1]* and Prof. Dr. Amina El-Shaibany[2]

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

***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.

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ABSTRACT
Chamomile has long been used in traditional medicine for the treatment of inflammation-related disorders. Gout is an inflammatory arthritis that belongs to a group of arthropathies called the 'crystalline arthropathies'. Gout is caused by a robust inflammatory response to *uric acid crystals* which occurs in the setting of hyperuricemia (high uric acid levels in the blood). Supersaturation of uric acid can lead to crystal accumulation and deposition in the joints and tissues to which the immune system reacts. Uric acid tophi (which occur in tophaceous gout) appear as hard nodules under the skin and can cause considerable destruction and discomfort. *Chamomile* is widely used throughout the world. Its primary uses are as a sedative, anxiolytic and antispasmodic, and as a treatment for mild skin irritation and inflammation. *Chamomile's* main active constituents are chamazulene, apigenin, and bisabolol. It was concluded that among the all formulations of *Chamomile* extract capsules the F3 was found to be as an optimized capsules according to drug release percentage 94% within 60 minutes, so the F3 was the best formulation of *Chamomile* extract capsules delivery system as an advanced phytotherapy approach for gout.

KEYWORDS: *Chamomile*, Extract, Capsules**,** Antigout, Phytotherapy.

INTRODUCTION

Background of Gout[1-9]

Gout is a form of arthritis caused by a build-up of uric acid in the blood. This builds up uric acid and causes crystals to form and accumulate in and around joints. What are Purines? Purines are natural chemical substances found in your body and in some foods and drinks. Uric acid is produced when the body breaks down purines. Uric acid is typically eliminated from your body in urine. In people with gout, this process is altered, so uric acid builds up in the blood forming crystals that settle in joints. Other foods and drinks influence the amount of uric acid in your blood, for example, fructose, a type of sugar, generates uric acid within minutes of being ingested.

The gout diet is low in purines, so while you can't control the number of purines that occur naturally in your body, you can control how much purines you consume, and therefore, lower the amount of uric acid your body produces. This will help control the pain from gout. It won't cure your gout and you may still need medication, but it can lower the risk of recurring gout attacks and slow the progression of joint damage. What are the Goals of the Gout Diet? The gout diet is designed to help you achieve a healthy weight and good eating habits, avoid foods high in purines, and control uric acid levels.

Gout is a type of arthritis. It is a disorder that results from the build-up of uric acid in the tissues or a join most often the joint of the big toe. If levels of uric acid are high for prolonged periods, needle-like crystals can start to form in your tissues, resulting in swollen, painful joints all of which are signs of inflammation. Uric acid is present in small amounts in our blood. It is made as our bodies break down natural substances called purines.

Gout arthritis usually come on suddenly. You may go to bed feeling fine but wake up with extreme joint pain. The first gout arthritis usually occurs in the large joint of the big toe. However, other joints and areas around the joints can be affected, like foot arches, ankles, heels and knees. Common symptoms include swelling, stiffness, tenderness, warmth and redness in and around joints. The

pain may last hours or weeks. The build-up of uric acid can look and feel like lumps under the skin (tophi). It can also collect in the kidneys and cause small, hard deposits (kidney stones).

Gout arthritis is caused by deposits of crystallized uric acid in the joint. Uric acid is present in the blood and eliminated in the urine, but in people who have gout, uric acid prolonged periods and crystallizes in the joints. Uric acid is the result of the breakdown of purines, chemicals that are found naturally in our bodies and in food. Some people develop gout because their kidneys have difficulty eliminating normal amounts of uric acid, while others related too much uric acid. Other factors that put a person at risk for developing gout include high blood pressure, diabetes, obesity, surgery, chemotherapy, stress, and certain medications and vitamins. Such as, the body's ability to remove uric acid can be negatively affected by taking aspirin, some diuretic medications, and the vitamin niacin. While gout is more common in men aged 40 to 60 years, it can occur in younger men and also occurs in women.

In diagnosing gout arthritis, your doctor will take your personal and family history and examine the affected joint. Laboratory tests and x-rays are sometimes ordered to determine if the inflammation is caused by something other than gout arthritis.

Initial treatment of gout arthritis typically includes the following: Medications. Prescription medications or injections are used to treat the pain, swelling, and inflammation. Dietary restrictions. Foods and beverages that are high in purines should be avoided, since purines are converted in the body to uric acid. Fluids. Drink plenty of water and other fluids each day, while also avoiding alcoholic beverages, which causes dehydration. Immobilize and elevate the foot. Avoid standing and walking to give your foot a rest. Also, elevate your foot (level with or slightly above the heart) to help reduce the swelling. Cortisone Injection. A combination of numbing and cortisone injected into the joint can help relieve pain and reduce the inflammation. The symptoms of gout arthritis t and the inflammatory process usually resolve in 3-10 days with treatment. If gout symptoms continue despite the initial treatment, or if repeated attacks occur, you may need to see your primary care physician for maintenance treatment that may involve daily medication. In cases of repeated episodes, the underlying problem must be addressed, as the build-up of uric acid over time can cause arthritic damage to the joint.

To understand more about your medicines and any risks or side effects that they may have, read the Consumer Medicine Information (CMI) leaflet that is available from your doctor or pharmacist.

Which foods should be avoided: As uric acid is made in the body from the breakdown of purines that come from your diet, it is advisable to reduce the amounts of foods that you eat that are high purines. High purine foods include: (avoid) offal - liver and kidneys, heart and sweetbreads, game - pheasant, rabbit, venison, oily fish - anchovies, herring, mackerel, sardines, sprats, whitebait, trout, seafood - especially mussels, crab, shrimps and other shellfish, fish roe, caviar, meat and yeast extracts - marmite, bovril, and commercial gravy as well as beer. Moderate purine foods (eat in moderation), meat - beef, lamb chicken, pork, poultry - chicken and duck, dried peas, beans and legumes - baked beans, kidney beans, soya beans and peas etc. Mushrooms and mycoprotein, some vegetables - asparagus, cauliflower, spinach, wholegrains - bran, oatbran, whole meal bread Low purine foods, dairy - milk, cheese, yoghurt, butter, eggs, bread, cereals, pasta, noodles, fruit and vegetables.

How much protein do you need: Generally, you need about 1g of protein per kg of body weight (70kg man only requires 70g of protein daily), unless you on a protein restricted diet e.g., some people with kidney disease may need to restrict their intake. Here are some examples of protein content of food: 100g chicken breast contains 22g protein, 100g cod fillet contains 21g protein. Large egg contains 6g, 30g hard cheese contains 8g protein, 30g cottage cheese contains 14g protein, 30g almonds contain 5g protein.

Recommended Foods to Eat: Fresh cherries, strawberries, blueberries, and other red-blue berries, bananas, celery, tomatoes, vegetables including kale, cabbage, parsley, green-leafy vegetables, foods high in vitamin C (red cabbage, red bell peppers, tangerines, mandarins, oranges, potatoes), drink fruit juices and purified water (8 glasses of water per day).

Natural or Alternative Therapies: There are many promises made for non-medical cures or treatments of gout. there is evidence that supplements such as celery seed or garlic are helpful in reducing the symptoms of gout. Because herbal, homeopathic, ayurvedic or Chinese medicines may affect the treatments prescribed by your doctor, please tell your GP and specialist what other treatments you are thinking about using. You may feel concerned that your doctor or other members of your healthcare team will disapprove of complementary therapies. However, it is very important to keep your healthcare team informed, even if they do not approve. Your healthcare team, particularly your doctor and pharmacist, can't give you the best professional advice without knowing all the treatments you are using. This includes vitamin supplements, herbal medicines and other therapies.

Fig. 1: Chamomile (Matricaria Recutita).

Pharmacological Activities of *Chamomile*[10-89]

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.

Combinations with chemically defined active substances or isolated constituents are not considered herbal preparations. Similarly, the European Medicine Evaluation Agency (EMEA) defines herbal preparations as medicinal products containing exclusively herbal drugs or herbal drug preparations as active substances. Several constituents with different pharmacological targets are involved in the therapeutic action of herbal preparations. This characteristic may be an advantage compared to single isolated compounds, especially when the underlying disease has a multifactorial etiology which is the case in many chronic illnesses.

Herbal preparations are comminuted or powdered plant material, extract, tinctures, fatty or essential oils, expressed juices, processed resins or gums and so forth prepared from different plant parts such as roots, bark, stems, leaves, and fruits whose production involves a fractional, purification, or concentration process.

Traditional medicine (TM)refers to health practices, approaches, knowledge and beliefs incorporating plant, animal and mineral based medicines, spiritual therapies, manual techniques and exercises, applied singularly or in combination to treat, diagnose prevent illnesses or maintain well-being (World Health Organization, 2003). According to WHO, as many as 80% of the world's population rely for their primary healthcare on traditional medicine, most of which are remedies made from plants. In South Africa, most people also associate traditional medicine with herbs.

The U. S. Food and Drug Administration (FDA) have classified the oil and extract of German and Roman *Chamomiles* as substances which named Generally Regarded as Safe (GRAS).

Chamomile preparations could be safe and provide therapeutic benefits. clearly that leaves are richer than flower and due to presence of all these nutrients and phytochemicals *Chamomile* cures many diseases.

Chamomile is widely used throughout the world as shown in Figure 1. Its primary uses are as a sedative, anxiolytic and antispasmodic, and as a treatment for mild skin irritation and inflammation. because the gout is a type of inflammatory arthritis the research concentration the studies that treatment of gout by *Chamomile* with other plant. *Chamomile's* main active constituents are chamazulene, apigenin, and bisabolol.

Chamomile is generally safe for consumption, although patients with hypersensitivity to ragweed and other family members of the Compositae family should use caution.

Historical and Popular uses of *Chamomile*

Chamomile has been used as an herbal medication since aged. *Chamomile* is one of the most widely used and well-documented medicinal plants in the world. It is included in the pharmacopoeia of 26 countries. The use of *Chamomile* as a medicinal plant dates back to ancient Greece and Rome. The name "*Chamomile*" comes from two Greek words meaning "ground apple" for its apple-like smell. The ancient Egyptians considered the herb a sacred gift from the sun god, and used it to alleviate fever and sun stroke. In the sixth century, it was used to treat insomnia, back pain, neuralgia, rheumatism, skin conditions, indigestion, flatulence, headaches, and gout.

In Europe it is considered a "cure all", and in Germany it is referred to as "alles zutraut", meaning "capable of anything". Although there are numerous varieties of *Chamomile*, the two most popular are Roman *Chamomile* (Anthemis nobilis) and German *Chamomile* (Matricaria recutita); both are from the Compositae family. German *Chamomile* is considered the more potent of the two, has received more scientific evaluation, and is more widely cultivated than Roman *Chamomile*; it is believed to possess anti-inflammatory, vulnerary, deodorant, bacteriostatic, antimicrobial, anticatarrhal, carminative, sedative, antiseptic, and spasmolytic properties.

Roman *Chamomile* is believed to possess carminative, antiemetic, antispasmodic, and sedative properties. *Chamomile* is used both internally and externally to treat an extensive list of conditions. It is used externally for wounds, ulcers, eczema, gout, skin irritations, neuralgia, sciatica, rheumatic pain, hemorrhoids, mastitis, and leg ulcers. Additionally, it is used externally to treat diaper rash, cracked nipples, chicken pox, poison ivy and conjunctivitis, and as a hair tint and conditioner. European oncologists use a *Chamomile* mouthwash called Kamillosan to treat chemotherapy-induced mouth sores. The German Commission E has approved *Chamomile* for external use for inflammation of the skin, mucous membranes and ano-genital area, bacterial skin diseases including those of the oral cavity and gums, and respiratory tract inflammation.

Chamomile is also extensively consumed as a tea or

tonic. It is used internally to treat anxiety, hysteria, nightmares, insomnia and other sleep problems, convulsions, and even delirium tremens. One of *Chamomile's* main roles is as a multipurpose digestive aid to treat gastrointestinal disturbances including flatulence, indigestion, diarrhea, anorexia, motion sickness, nausea, and vomiting. *Chamomile* is thought to heal ulcers and act as an herbal bitter to stimulate the liver. In children it is used to treat colic, croup, and fevers. In women's health, it is used as an emmenagogue and a uterine tonic. *Chamomile's* essential oil is also a treatment for malaria and parasitic worm infections, cystitis, colds, and flu. The German Commission E recommends *Chamomile* to treat gastrointestinal spasms and inflammatory diseases of the gastrointestinal tract.

Chamomile (*Matricaria Chamomilla L.)* is a medicinal herb native to southern and eastern Europe; belongs to the Asteraceae family. Germany, Hungary, France, Russia, Yugoslavia and Brazil are the countries which cultivate *Chamomile* on large scale. The hollow, bright gold cones of the flowers are packed with disc or tubular florets and are ringed with about fifteen white ray or ligulate florets, widely as *Chamomile*. The two most common species of *Chamomile* are German *Chamomile* (*Marticaria Recutita*) and Roman *Chamomile* (*Chamaemelum Nobile*). The terpenoids and flavonoids are thought to be responsible for *Chamomile's* medicinal properties.

Matricaria Recutita L. (syn. M. Chamomilla L., Chamomilla recutita L. Rauschert) is known as true *Chamomile* or German *Chamomile* and Chamaemelum nobile (L.) All. (syn. Anthemis nobilis L.) is known as Roman *Chamomile*. The biological activity of chamomile is mainly due to the flavonoids apigenin, luteolin, quercetin, patuletin and essential oil constituents such as α-bisabolol and its oxides and azulenes. There are several *Chamomile* chemocultivars. *Chamomile* has anti-inflammatory, deodorant, bacteriostatic, antimicrobial, carminative, sedative, antiseptic, anticatarrhal and spasmolytic properties. It is used to treat sleep problems.

The pervious study mainly focuses on the nutraceutical's potential of *Chamomile* leaf and flower of this plant. The nutrient contains of the leaf and flower power was determined by various methods. The phytochemicals screening of the leaf and flower aqueous extract was performed by different procedure. Leaf of this plant is rich in carbohydrate, protein, fat and also rich in vitamin C, iron, zinc and calcium. Whereas flower is rich in moisture and fiber as compared to leaf. The aqueous extract of leaf of *Chamomile* showed presence of steroids, terpenoids, flavonoids, tannins and saponins and flower were lacked in alkaloids, saponins, gale tin and phenolic compounds. Leaves, flowers and stems of *Chamomile* are used as anti-oxidant, analgesic, antiviral, anti-inflammatory, anti-septic, anti-diabetic, anti-proliferative, anti-bacterial activities and many more diseases.

In another previous study intended to focus on the possible anti-inflammatory pharmacological mechanisms of MC preparations in the treatment of gouty arthritis and the constituents of MC responsible for its effects. The medicinal preparations of MC are composed of several classes of biologically active compounds with an inhibitory effect on inflammation including essential oils and flavonoids. Apigenin, quercetin and luteolin are flavonoids, which exhibit their anti-inflammatory effects via different mechanisms. Apigenin exhibits anti-inflammatory activity via inhibition of proinflammatory cytokines production. Luteolin suppresses production of nitric oxide (NO), prostaglandin E2 and expression of inducible NO synthase (iNOS) and cyclooxygenase-2 – which are all associated with inflammatory responses. In addition, Luteolin along with quercetin, inhibit xanthine oxidase (XO) enzyme. There are also additional components of the MC preparations which play a role in its anti-inflammatory action via other pathways.

Chamomile has long been used in traditional medicine for the treatment of inflammation-related disorders. In early study it was demonstrate that *Chamomile* inhibits NO production and iNOS gene expression by inhibiting RelA/p65 activation and supports the utilization of *Chamomile* as an effective anti-inflammatory agent. The fact that NF-κ B/Rel is negatively regulated by *Chamomile* is important, because this transcription factor plays a critical role in the regulation of a variety of genes that are involved in inflammatory responses. Since *Chamomile* is a nontoxic and pharmacologically active compound that has demonstrable inhibitory effects on iNOS gene expression, and since NO plays an important role in mediating inflammatory responses, supports the utilization of *Chamomile* as a potentially effective therapeutic anti-inflammatory agent.

The dried flowers of *Chamomile* contain many terpenoids and flavonoids contributing to its medicinal properties. *Chamomile* preparations are commonly used for many human ailments such as hay fever, inflammation, muscle spasms, menstrual disorders, insomnia, ulcers, wounds, gastrointestinal disorders, rheumatic pain, and hemorrhoids. Essential oils of *Chamomile* are used extensively in cosmetics and aromatherapy. Many different preparations of *Chamomile* have been developed, the most popular of which is in the form of herbal tea consumed more than one million cups per day. In previous study that describe the use of *Chamomile* in traditional medicine with regard to evaluating its curative and preventive properties, highlight recent findings for its development as a therapeutic agent promoting human health.

Traditional use of *Chamomile* has been used for centuries as an anti-inflammatory, antioxidant, mild astringent and healing medicine. As a traditional medicine, it is used to treat wounds, ulcers, eczema,

gout, skin irritations, bruises, burns, canker sores, neuralgia, sciatica, rheumatic pain, hemorrhoids, mastitis and other ailments. Externally, *Chamomile* has been used to treat diaper rash, cracked nipples, chicken pox, ear and eye infections, disorders of the eyes including blocked tear ducts, conjunctivitis, nasal inflammation and poison. *Chamomile* is widely used to treat inflammations of the skin and mucous membranes, and for various bacterial infections of the skin, oral cavity and gums, and respiratory tract. *Chamomile* in the form of an aqueous extract has been frequently used as a mild sedative to calm nerves and reduce anxiety, to treat hysteria, nightmares, insomnia and other sleep problems. *Chamomile* has been valued as a digestive relaxant and has been used to treat various gastrointestinal disturbances including flatulence, indigestion, diarrhea, anorexia, motion sickness, nausea, and vomiting. *Chamomile* has also been used to treat colic, croup, and fevers in children. It has been used as an emmenagogue and a uterine tonic in women. It is also effective in arthritis, back pain, bedsores and stomach cramps.

Chamomile has a long history of traditional medicinal uses. The two commonly used varieties with therapeutic applications are German *Chamomile* known as Matricaria chamomilla L. and Roman *Chamomile* or Chamaemelum nobile L. The plant contains many components, namely, flavonoids, terpenoids, and coumarins, which are responsible for its medicinal properties. The pervious review studies discuss recent developments that help in establishing its role as a therapeutic agent in various areas as an anti-inflammatory, antioxidant, analgesic, antimicrobial, hepatoprotective, anti-allergic, anticancer, and anti-hypertensive agent. Not much is known about its role in the treatment of CNS disorders and metabolic syndromes, which are also discussed. The chemical components responsible for the therapeutic activity and the respective mechanism of action are also elaborated.

It has been reported by many previous studies have comprehensively detailed different therapeutic applications, suggesting *Chamomile* as a promising herb. Therefore, to enhance the safety and efficacy of *Chamomile*, it is imperative to utilize concepts of novel delivery. Future Prospects The review highlights the biological activities exhibited by different chemical nanocapsules, liposomes, etc., which will enhance its clinical acceptability and favourable application in medicine.

The Capsule Delivery System

Capsules offer many advantages: Capsules, because of their elongated shape, are easy to swallow, which is one reason for the number of capsule- shaped tablets manufactured today, flexibility of formulation is another advantage of the capsule dosage form. However, the biggest formulation advantage of capsules is that there is less need for additional excipients, since capsules are tasteless, they effectively mask any unpleasant taste or odor of their contents, they offer rapid release characteristics, due to the rapid dissolution rate of the capsules, Herbal capsules are solid dosage forms containing drug and usually, appropriate filler (s) enclosed in a gelatin container. Capsules may be available in hard gelatin for dry powdered herbal ingredients or granules or soft gelatin shells for herbal oils and for herbal ingredients that are dissolved or suspended in oil. The gelatin shell readily ruptures and dissolves following oral administration. Drugs are normally more readily released from capsules compared to tablets. Capsules may help mask the unpleasant taste of its contents and uniformity of dosage can be relatively readily achieved. Herbal capsules normally consist of hard-shelled gelatin capsules with the plant material finely milled and sifted and filled into shell or extracts of the herbal material(s) with appropriate excipients such as fillers.

In the present study the *Chamomile* extract powder solid dosage form of *Chamomile* capsules delivery system was prepared and evaluated as an advanced phytotherapy approach for gout.

MATERIALS AND METHODS

The extract of *Chamomile* was prepared and gift from (Prof Dr. Amina El-Shaibany, Professor Dr. of Pharmacognosy, Department of Pharmacognosy, Faculty of Pharmacy, Sana'a University, Sana'a, Yemen). Hard Gelatin Capsules (Size 0), Diluents, Lubricant, Hydrochloric Acid (0.1NHCl), Phosphate Buffer Solution, Ethanol and Methanol were obtained from Sigma Aldrich. All chemicals used were all of analytical grade and other materials were gift from (Shaphaco Pharmaceutical Industry Company-Yemen).

Formulation and Evaluation of *Chamomile* Extract [45-152]

Determination of The Organoleptic Properties of Extract

The following organoleptic properties of the plant materials were assessed: physical appearance, odor and taste. For these samples of *Chamomile* extracts were inspected and assessed using the natural senses (e.g. eyes, nose, mouth).

Determination of The Solubility of Extract

The solubility of a substance fundamentally depends on the solvent used as well as on temperature and pressure. The extent of solubility of a substance in a specific solvent is measured as the saturation concentration where adding more solute does not increase its concentration in the solution. Oral ingestion is the most convenient and commonly employed route of drug delivery due to its ease of administration, high patient compliance, cost-effectiveness, least sterility constraints, and flexibility in the design of dosage form. As a result, many of the generic drug companies are inclined more to produce bioequivalent oral drug products. So, the solubility

application according to standard parameters of solubility as shown in Table 1.

Table 1: Standard of Approximate Solubility.

Description	Part of The Solvent Required Per Part of Solute
Very Soluble	Less than 1
Freely Soluble	From 1 to 10
Soluble	From 10 to 30
Sparingly Soluble	From 30 to 100
Slightly Soluble	From 100 to 1000
Very slightly Soluble	From 1000 to 10,000
Practically Insoluble	More than 10,000

Determination of The Flowability of Extract

Preformulation parameters like bulk density, tapped density, carr's index, A known quantity of powder was poured into the measuring cylinder carefully level the powder without compacting, if necessary and read the unsettled apparent volume, Vo, to the nearest graduated unit as shown in Table 2.

Calculate the bulk density, in gm per ml, by the formula.

Bulk density = Bulk Mass/ Bulk Volume

Carr's compressibility index.

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

Table 2: Carr's Index of Powder Flowability.

Carr's Index%	Type of Flow
5 -15	Excellent
12 – 16	Good
18 – 21	Fair to Passable
23 – 35	Poor
33 – 38	Very Poor
>40	Extremely Poor

Formulation of *Chamomile* Extract Capsules

A uniform powder is obtained by mixing the ***Chamomile*** extract of with the appropriate adsorbent, diluents and lubricant, the materials filled into the capsules as shown in Table 3.

Table 3: Formulation of *Chamomile* Extract Capsules.

Ingredients	Quantity Per Capsule (mg) Formulation Code		
	F1	**F2**	**F3**
Chamomile Extract	15%	15%	15%
Diluent I	59%	25%	45%
Diluent II	25%	59%	39%
Lubricant	1%	1%	1%

Evaluation of *Chamomile* Extract Capsules

Determination of Uniformity of Weight and The Amount of *Chamomile* Capsules

For the determination of the uniformity of weight, the British Pharmacopoeia method was used. In which Twenty of the *Chamomile* capsules prepared. 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, 20% of *Chamomile* extract was to be filled in one capsule. 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 *Chamomile* Extract Capsules

The presence of water plays an important role in the physical and chemical stability of the active pharmaceutical ingredients, and pharmaceutical preparations, because they may lead to their degradation. Water in pharmaceutical substances and preparations, provides a favorable environment for bacterial growth. Once a composition which contains a certain number of bacteria enters the organism, in the gastrointestinal tract may come to the death of bacteria and release of endotoxin. Even a small amount of endotoxin in the body

causes the formation of antibodies against the endotoxin. During gastrointestinal crises, the blood stream can be penetrated by a large amount of endotoxin, which leads to an anaphylactic reaction, which results in a hard shock. The moisture content of the material is a decisive economic factor both in production and in sales. This is one of the main factors that influences the course of production and stability of the finished product, determining the quality and prices of many pharmaceutical products. Therefore, the presence of water in the pharmaceutical substances affect; quality of the finished product, commercial reasons, i.e. process ability of the product, storage of the finished product, accuracy of the finished product, analytical indicators on the dry matter, since it is necessary to know the water content for their calculations.

In-Vitro Dissolution Studies of *Chamomile* Extract Capsules

The dissolution test measures the rate at which a drug is released into solution from a dosage form and is used as an indication of the bioavailability of a pharmaceutical product and of product quality. In the present study the basket method was used. The quantitation of the amount of extract dissolved was measured based on UV absorbance measured at 270 nm, the wavelengths for maximum UV absorbance of solutions of the *Chamomile* extract determined by using a UV- Vis Spectrophotometer. For the dissolution study the following requirements and Procedure were used: Apparatus: Basket. Medium: 0.1N HCl. Volume of medium: 900ml.Temperature: 37±0.5°C. Rotation speed: 50 rpm. Dissolution time: 15, 30, 45 and 60 minutes.

900 ml of 0.1N HCl was degassed, introduced into the vessel of the apparatus, warmed to 37±0.5°C in the water bath. One capsule was placed in each vessel, the basket was lowered into position and the apparatus were operated immediately at the rotation speed 50 rpm. At various time points, viz. at 15, 30, 45 and 60 minutes after start, 3 ml samples of the medium were withdrawn from a point half- way between the surface of the dissolution medium and the top of the rotating basket and not less than 10 mm from the wall of the vessel. Each time the withdrawn medium was immediately replaced by 3 ml of 0.1N HCl introduced into the vessel.

RESULTS AND DISCUSSION

The Organoleptic Properties of *Chamomile* Extract

As shown in Table 4, the organoleptic properties of extract.

Table 4: The Organoleptic Properties of *Chamomile* Extract.

Properties	*Chamomile* Extract
Physical Appearance	Small powder
Color	Brown Darker
Odor	Characteristic Odor
Taste	Bitter

The bitter taste and characteristic odor 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 *Chamomile* Extract

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 *Chamomile* extract show that the extract is sparingly soluble in water as shown in Table 5.

Table 5: Evaluation Parameters of *Chamomile* Extract.

Testing	*Chamomile*
The Solubility of Extract	Sparingly Soluble in Water
Carr's Index (%)	11%
Particle Size	Coarse Powder
The Moisture Content (%)	1.5%

The Flowability of Extract

The Carr's index of compressibility for *Chamomile* extract is 11% show that the *Chamomile* extract powders can all be categorized as having excellent flowability for the manufacture of capsule dosage form as shown in Table 5.

Moisture Content of *Chamomile* Extract Capsules

The results of these tests are indicated that the moisture level of the contents of *Chamomile* capsules when analyzed in the pre-formulation study, the moisture content for *Chamomile* extract was found to be 2%, as shown in Table 5.

The Uniformity of Weight and The Amount of *Chamomile* Extract Capsules

The average deviation in weight from average for *Chamomile* capsules were found to be 0.80% and average total content per capsule was 100.11%, within the limit on the acceptable deviation in weight from average for capsules therefore, mentioned results thus indicated that the *Chamomile* capsules are within the limit of the British Pharmacopoeia specifications.

***In-Vitro* Dissolution Studies of *Chamomile* Extract Capsules**

Table 6: The Drug Release Percentage of *Chamomile* Extract Capsules.

	Formulation Code			
Drug Release %		**F1**	**F2**	**F3**
Time (min)	15	25	30	72
	30	46	50	80
	45	63	65	93
	60	75	80	94

The *in-vitro* dissolution percentage of *Chamomile* extract capsules is one important of the results of dissolved active ingredient, *Chamomile* extract, as shown in Table 6. The results of formulation have shown that the drug release of F3 was found to be 80% within 30 minutes in buffer medium. The results of formulation have shown that the drug release of F3 was found to be 93% within 45 minutes in buffer medium. The results of formulation have shown that the drug release of F3 was found to be 94% within 60 minutes in buffer medium.

CONCLUSION

Chamomile has been used as an herbal medication since aged. It was concluded that among the all formulations of *Chamomile* extract capsules the F3 was found to be as an optimized capsules according to drug release percentage 94% within 60 minutes, so the F3 was the best formulation of *Chamomile* extract capsules delivery system as an advanced phytotherapy approach for gout.

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REFERENCES

1. Gout: Introduction to Gout (hopkinsarthritis.org).
2. Gout Treatment: Medications and Lifestyle Adjustments to Lower Uric Acid (hopkinsarthritis.org).
3. Gout Symptoms and Diagnosis | Johns Hopkins Arthritis Center.
4. Hirayama A, et al. Assessing the Cardiovascular Risk between Celecoxib and Nonselective Non-Steroidal Anti-Inflammatory Drugs in Patients with Rheumatoid Arthritis and Osteoarthritis. Circ J., 2014; 78(1): 194-205.
5. Venkatachalam J, Natesan M, Eswaran M, Johnson AK, Bharath V, Singh Z. Prevalence of Osteoarthritis of Knee Joint Among Adult Population in a Rural Area of Kanchipuram District, Tamil Nadu. Indian J Public Health., 2018; 62: 117-22.
6. Fransen M, Bridgett L, March L, Hoy D, Penserga E, Brooks P, et al. The Epidemiology of Osteoarthritis in Asia. International Journal of Rhematoilogy Disorders., 2011; 14: 113-21.
7. Sharma MK, Swami HM, Bhatia V. Verma A, Bhatia s. Kaur G. An Epidemiological Study of Co-Relates of Osteoarthritis in Geriatric Population of Chandigarh. Indian J Community Med., 2013; 32: 77.
8. Salaffi F, Ciapetti A, Carotti M. The Sources of Pain in Osteoarthritis: A Pathophysiological Review. Reumatismo., 2014; 6; 66(1): 57-71.
9. Crofford LJ. Use of NSAIDs in Treating Patients with Arthritis. Arthritis Research & Therapy., 2013 Jul; 15(3): 1.
10. Sharafzadeh S, Alizadeh O. German and Roman Chamomile. Journal of Applied Pharmaceutical Science., 2011; 01(10): 01-05.
11. Ghavimi H, Shayanfar A, Hamedeyazdan S, Shiva A, Garjani A.Chamomile: An ancient pain remedy and a modern gout relief - A hypothesis.African Journal of Pharmacy and Pharmacology., 2012; 6(8): 508-511.
12. Bhaskaran N, Shukla S, Srivastava J, Gupta S. Chamomile, an anti-inflammatory agent inhibits inducible nitric oxide synthase expression by blocking RelA/p65 activity. Int J Mol Med., 2010; 26(6): 935–940.
13. Srivastava JK, Eswar Shankar E, Sanjay Gupta S. Chamomile: A herbal medicine of the past with bright future. Mol Med Report., 2010; 1; 3(6): 895–901.
14. Sah A, Naseef PP, Kuruniyan MS, Jain GK, Zakir F, Aggarwal G. A Comprehensive Study of Therapeutic Applications of Chamomile. Pharmaceuticals., 2022; 15: 1284.
15. Bansal P, Gupta V, Mittal P, Khokra SL, Kaushik D. Pharmacological Potential of Matricaria recutita—A Review. Int J Pharm Sci Drug Res., 2010; 2: 12–16.
16. Chamomile. In Drugs and Lactation Database (LactMed); National Library of Medicine: Bethesda MD USA. 2021.
17. Salamon I. The Slovak Gene Pool of German Chamomile (Matricaria recutita L.) and Comparison in its Parameters. Hortic Sci., 2018; 31: 70–75.
18. Tsivelika N, Irakli M, Mavromatis A, Chatzopoulou P, Karioti, A. Phenolic Profile by HPLC-PDA-MS of Greek Chamomile Populations and Commercial Varieties and Their Antioxidant Activity. Foods., 2021; 10: 2345.
19. Singh O, Khanam Z, Misra N, Srivastava MK. Chamomile (Matricaria chamomilla L.): An Overview. Pharmacogn Rev., 2011; 5: 82–95.
20. Pino JA, Bayat F, Marbot R, Aguero J. Essential Oil of Chamomile Chamomilla recutita (L.) Rausch. From Iran. J Essent Oil Res., 2002; 14: 407–408.
21. Catani MV, Rinaldi F, Tullio V, Gasperi V, Savini I. Comparative Analysis of Phenolic Composition of Six Commercially Available Chamomile (Matricaria chamomilla L.) Extracts: Potential Biological

Implications. Int J Mol Sci., 2021; 22: 10601.
22. Mulinacci N, Romani A, Pinelli P, Vinvieri FF, Prucher D. Characterisation of M. recutita L. Flower Extract by HPLCMS and HPLC-DAD Analysis. Chromatographia., 2000; 51: 301–307.
23. Chauhan ES, Aishwarya J. Nutraceutical Analysis of Marticariarecutita (Chamomile) Dried Leaves and Flower Powder and Comparison Between Them. Int J Phytomed., 2018; 10: 111–114.
24. Matos FJA, Machado MIL, Alencar JW, Craveiro AA. Constituents of Brazilian Chamomile Oil. J Essent Oil Res., 2011; 5: 337–339.
25. Haghi G, Hatami A, Safaei A, Mehran M. Analysis of Phenolic Compounds in Matricaria Chamomilla and its Extracts by UPLC-UV. Res Pharm Sci., 2014; 9: 31–37.
26. Ling C, Zheng L, Yu X, Wang H, Wang C, Wu H, Zhang J, Yao P, Tai Y, Yuan Y. Cloning and Functional Analysis of three Aphid Alarm Pheromone Genes from German Chamomile (Matricaria chamomilla L.). Plant Sci., 2020; 294: 110463.
27. Lee SH, Heo Y, Kim YC. Effect of German Chamomile Oil Application on Alleviating Atopic Dermatitis-Like Immune Alterations in Mice. J Vet Sci., 2010; 11: 35–41.
28. Weber L, Kuck K, Jürgenliemk G, Heilmann J, Lipowicz B, Vissiennon C. Anti-Inflammatory and Barrier-Stabilising Effects of Myrrh, Coffee Charcoal and Chamomile Flower Extract in a Co-Culture Cell Model of the Intestinal Mucosa. Biomolecules., 2020; 10: 1033.
29. Bhaskaran N, Shukla S, Srivastava JK, Gupta S. Chamomile: An Anti-Inflammatory Agent Inhibits Inducible Nitric Oxide Synthase Expression by Blocking RelA/p65 Activity. Int J Mol Med., 2010; 26: 935–940.
30. Flemming M, Kraus B, Rascle A, Jürgenliemk G, Fuchs S, Fürst R, Heilmann J. Revisited Anti-Inflammatory Activity of Matricine *In-Vitro*: Comparison with Chamazulene. Fitoterapia., 2015; 106: 122–128.
31. Wang W, Yue RF, Jin Z, He LM, Shen R, Du D, Tang YZ. Efficiency Comparison of Apigenin-7-O-glucoside and Trolox in Antioxidative Stress and Anti-Inflammatory Properties. J Pharm Pharmacol., 2020; 72: 1645–1656.
32. Chandrashekhar VM, Halagali KS, Nidavani RB, Shalavadi MH, Biradar BS, Biswas D, Muchchandi IS. Anti-Allergic Activity of German Chamomile (Matricaria recutita L.) in Mast Cell Mediated Allergy Model. J Ethnopharmacol., 2011; 137: 336–340.
33. Mekonnen A, Yitayew B, Tesema A, Taddese S. *In-Vitro* Antimicrobial Activity of Essential Oil of Thymus Schimperi, Matricaria Chamomilla, Eucalyptus Globulus, and Rosmarinus Officinalis. Int J Microbiol., 2016; 95: 693.
34. Kazemian H, Ghafourian S, Sadeghifard N, Houshmandfar R, Badakhsh B, Taji A, Shavalipour A, Mohebi R, EbrahimSaraie HS, Houri H, et al. *In - Vivo* Antibacterial and Wound Healing Activities of Roman Chamomile (Chamaemelumnobile). Infect Disord Drug Targets., 2018; 18: 41–45.
35. Koch C, Reichling J, Kehm R, Sharaf MM, Zentgraf H, Schneele J, Schnitzler P. Efficacy of Anise Oil, Dwarf-Pine Oil and Chamomile Oil Against Thymidine-Kinase-Positive and Thymidine-Kinase-Negative Herpesviruses. J Pharm Pharmacol., 2008; 60: 1545–1550.
36. Chaves P, Hocayen P, Dallazen JL, de Paula Werner MF, Iacomini M, Andreatini R, Cordeiro L. Chamomile Tea: Source of a Glucuronoxylan with Antinociceptive, Sedative and Aanxiolytic-Like Effects. Int J Biol Macromol., 2020; 164: 1675–1682.
37. Amsterdam JD, Li QS, Xie SX, Mao JJ. Putative Antidepressant Effect of Chamomile (Matricaria chamomilla L.) Oral Extract in Subjects with Comorbid Generalized Anxiety Disorder and Depression. J Altern Complement Med., 2020; 26: 813–819.
38. Sebai H, Jabri MA, Souli A, Hosni K, Rtibi K, Tebourbi O, El-Benna J, Sakly M. Chemical Composition, Antioxidant Properties and Hepatoprotective Effects of Chamomile (Matricariarecutita L.) Decoction Extract Against Alcohol-Induced Oxidative Stress in Rat. Gen Physiol Biophys., 2015; 34: 263–275.
39. Zhao J, Khan SI, Wang M, Vasquez Y, Yang MH, Avula B, Wang YH, Avonto C, Smillie TJ, Khan IA. Octulosonic Acid Derivatives from Roman Chamomile (Chamaemelumnobile) with Activities Against Inflammation and Metabolic Disorder. J Nat Prod., 2014; 77: 509–515.
40. Hajaji S, Sifaoui I, López-Arencibia A, Reyes-Batlle M, Valladares B, Pinero JE, Lorenzo-Morales J, Akkari H. Amoebicidal Activity of α-Bisabolol, the Mmain Sesquiterpene in Chamomile (Matricariarecutita L.) Essential Oil Against the Trophozoite Stage of Acanthamoeba Castellani Neff. Acta Parasitol., 2017; 62: 290–295.
41. Hajaji S, Sifaoui I, López-Arencibia A, Reyes-Batlle M, Jiménez IA, Bazzocchi IL, Valladares B, Akkari H, LorenzoMorales J, Piñero JE. Leishmanicidal Activity of α-Bisabolol from Tunisian Chamomile Essential Oil. Parasitol Res., 2018; 117: 2855–2867.
42. Kobayashi Y, Takahashi R, Ogino F. Antipruritic Effect of the Single Oral Administration of German Chamomile Flower Extract and its Combined Effect with Antiallergic Agents in DDY Mice. J Ethnopharmacol., 2005; 101: 308–312.
43. Khalesi ZB, Beiranvand SP, Bokaie M. Efficacy of Chamomile in the Treatment of Premenstrual Syndrome: A Systematic Review. J Pharmacopunct., 2019; 22: 204–209.
44. Vissiennon C, Goos KH, Arnhold J, Nieber K. Mechanisms on Spasmolytic and Anti-Inflammatory Effects of a Herbal Medicinal Product Consisting of Myrrh, Chamomile Flower, and Coffee Charcoal.

Wien Med Wochenschr Suppl., 2017; 167: 169–176.
45. WHO, Good Manufacturing Practices. In WHO Expert Committee on Specifications for Pharmaceutical Preparations and Supplementary Guidelines for the Manufacture of Herbal Medicinal Products, 34th edition, Geneva, Switzerland.,1996; 109 – 113.
46. Busse W, The Significance of Quality for Efficacy and Safety of Herbal Medicinal Products, 34, Drug Information Association Inc USA., 2000.
47. Aulton M. E. Pharmaceutics: The Science of Dosage Form Design, 2nd Edition.Edinburg: Churchill Livingstone., 2002; Pages 205-210, 365-395.
48. Winfield AJ, Rees AJ. and Smith I. Pharmaceutical Practice. Churchill Livingstone., 2009; Page 337.
49. Taylor AF, Attwood D. Physicochemical Principles of Pharmacy. Pharmaceutical Press, London., 2006; Page 34.
50. Jones BE. Pharmaceutical Capsules 2nd edition. Edited by Podczeck F, Jones B E. Pharmaceutical Press. London., 2004; pp1, 2, 9,17, 23, 91,103,119,120, 242, 449.
51. Winfield AJ, Rees AJ, Smith I. Pharmaceutical Practice. London: Churchill Livingstone; 2009.
52. Bayor MT, Johnson R, Gbedema SY. The oral Capsule-The Most Appropriate Dosage Form for Croton Membranous. Int J Pharm Sci Res., 2011; 2: 55-62.
53. Hoffman D. Medical Herbalism: The Science and Practice of Herbal Medicine. Vermont: Healing Arts Press., 2003.
54. Aulton ME. Aulton's Pharmaceutics-The Design and Manufacture of Medicines. 3rd Ed. London: Churchill Livingstone; 2007.
55. Johnson R, Bayor MT, Adotey J. Formulation and Evaluation of Bridelia Ferruginea and Canthium Glabriflorum Herbal Capsules. J Herbal Med Plants., 2010; 1: 18-22.
56. McKay DL, Blumberg JB. A review of the bioactivity and potential health benefits of chamomile tea (Matricaria recutita L). Phytother Res., 2006; 20: 519–530.
57. Srivastava JK, Gupta S. Antiproliferative and Apoptotic Effects of Chamomile Extract in Various Human Cancer Cells. J Agric Food Chem., 2007; 55: 9470–9478.
58. Speisky H, Rocco C, Carrasco C, Lissi EA, López-Alarcón C. Antioxidant screening of medicinal herbal teas. Phytother Res., 2006; 20: 462–467.
59. Ganzera M, Schneider P, Stuppner H. Inhibitory effects of the essential oil of chamomile (Matricaria recutita) and its major constituents on human cytochrome P450 enzymes. Life Sci., 2006; 78: 856–861.
60. Ross SM. Chamomile: a spoonful of medicine. Holistic Nursing Practice., 2008; 22: 56–57.
61. Babenko NA, Shakhova EG. Effects of Chamomilla recutita flavonoids on age-related liver sphingolipid turnover in rats. Exp Gerontol., 2006; 41: 32–39.
62. Lee KG, Shibamoto T. Determination of antioxidant potential of volatile extracts isolated from various herbs and spices. J Agric Food Chem., 2002; 50: 4947–4952.
63. Srivastava, JK.; Gupta, S. Health promoting benefits of chamomile in the elderly population. In: Watson, Ronald R., editor. Complementary and Alternative Therapies in the Aging Population. Elsevier Inc., Academic Press; 2009.
64. Srivastava JK, Pandey M, Gupta S. Chamomile, a novel and selective COX-2 inhibitor with anti-inflammatory activity. Life Sci., 2009; 85: 663–669.
65. Bradford MM. A rapid and sensitive method for the quantitation of microgram quantities of protein utilizing the principle of protein-dye binding. Anal Biochem., 1976; 72: 248–254.
66. Shukla S, MacLennan GT, Fu P, et al. Nuclear Factor-κB/p65 (Rel A) Is Constitutively Activated in Human Prostate Adenocarcinoma and Correlates with Disease Progression. Neoplasia., 2004; 6: 390–400.
67. Newman DJ, Cragg GM, Snader KM. Natural products as sources of new drugs over the period 1981–2002. J Nat Prod., 2003; 66: 1022–1037.
68. Koehn FE, Carter GT. The evolving role of natural products in drug discovery. Nat Rev Drug Discov., 2005; 4: 206–220.
69. Jones WP, Chin YW, Kinghorn AD. The role of pharmacognosy in modern medicine and pharmacy. Curr Drug Targets., 2006; 7: 247–264.
70. Philip RB. Herbal remedies: the good, the bad, and the ugly. J. Comp. Integ. Med 2004; 1: 1–11.
71. Fabricant DS, Farnsworth NR. The value of plants used in traditional medicine for drug discovery. Environ Health Perspect., 2001; 109: 69–75.
72. Hadley SK, Petry JJ. Medicinal herbs: A primer for Primary Care Hosp Prac. Hosp Pract (Minneap)., 1999; 34: 105–116.
73. Astin JA, Pelletier KR, Marie A, Haskell WL. Complementary and Alternative medicine use among elderly persons: One year analysis of Blue Shield medicare supplement. J Gerontol., 2000; 55: M4– M9.
74. Hansen HV, Christensen KIb. The common chamomile and the scentless may weed revisited. Taxon. International Association for Plant Taxonomy., 2009; 58: 261–264.
75. Lemberkovics E, Kéry A, Marczal G, Simándi B, Szöke E. Phytochemical evaluation of essential oils, medicinal plants and their preparations. Acta Pharm Hung., 1998; 68: 141–149.
76. Baser KH, Demirci B, Iscan G, et al. The essential oil constituents and antimicrobial activity of Anthemis aciphylla BOISS. Var. discoidea BOISS. Chem. Pharm. Bull. (Tokyo)., 2006; 54: 222– 225.
77. Mazokopakis EE, Vrentzos GE, Papadakis JA, Babalis DE, Ganotakis ES. Wild chamomile (Matricaria recutita L.) mouthwashes in methotrexate-induced oral mucositis. Phytomedicine., 2005; 12: 25–27.
78. Shukla S, Mishra A, Fu P, MacLennan GT, Resnick

MI, Gupta S. Up-regulation of insulin-like growth factor binding protein-3 by apigenin leads to growth inhibition and apoptosis of 22Rv1 xenograft in athymic nude mice. FASEB J., 2005; 19: 2042–2044.
79. Gould L, Reddy CV, Gomprecht RF. Cardiac effects of chamomile tea. J Clin Pharmacol., 1973; 11: 475–479.
80. Gardiner P. Complementary, Holistic, and Integrative Medicine: Chamomile. Pediatr Rev., 2007; 28: 16–18.
81. Zeggwagh NA, Moufid A, Michel JB, Eddouks M. Hypotensive effect of Chamaemelum nobile aqueous extract in spontaneously hypertensive rats. Clin Exp Hypertens., 2009; 31: 440–450.
82. Ramos-e-Silva M, Ferreira AF, Bibas R, Carneiro S. Clinical evaluation of fluid extract of Chamomilla recutita for oral aphthae. J Drugs Dermatol., 2006; 5: 612–617.
83. Graf J. Herbal anti-inflammatory agents for skin disease. Skin Therapy Letter., 2000; 5: 3–5.
84. Tubaro A, Zilli C, Redaelli C, Della Loggia R. Evaluation of anti-inflammatory activity of a chamomile extract after topical application. Planta Med., 1984; 50: 359.
85. Kyokong O, Charuluxananan S, Muangmingsuk V. Efficacy of chamomile-extract spray for prevention of post-operative sore throat. J Med AssocThai., 2002; 85: 180–185.
86. Benetti C, Manganelli F. Clinical experiences in the pharmacological treatment of vaginitis with a chamomile-extract vaginal douche. Minerva Ginecol., 1985; 37: 799–801.
87. Nayak BS, Raju SS, Rao AV. Wound healing activity of Matricaria recutita L. extract. J Wound Care., 2007; 16: 298–302.
88. Alburyhi MM. Doctor Thesis, Faculty of Pharmacy, Cairo University., 2009.
89. Saif AA, Alburyhi MM, Noman MA, Yahya TA, Al-Ghorafi MA. Famotidine-Excipient Compatibility Studies for Advanced Drug delivery Systems Development. World Journal of Pharmaceutical Research., 2024; 13(18): 1346-1408.
90. Alburyhi MM, Noman MA, Saif AA, Al-Ghorafi MA, Al Khawlani MA, Yahya TAA. Formulation and Evaluation of Anti-acne Spironolactone Emulgel Novel Trend in Topical Drug Delivery System. World Journal of Pharmaceutical Research., 2023; 12(22): 96-119.
91. Alburyhi MM, Hamidaddin MA, Noman MA, Saif AA, Yahya TA, Al-Ghorafi MA. Rivaroxaban - Excipient Compatibility Studies for Advanced Drug delivery Systems Development. European Journal of Pharmaceutical and Medical Research., 2024; 11(9): 370-404.
92. 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.
93. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of Pandanus Odoratissimus Extract Capsules Delivery System as an Advanced Phytotherapy Approach for Breast Cancer. World Journal of Pharmaceutical Research., 2024; 13(8): 1092-1112.
94. Alburyhi MM, Noman MA, Saif AA, Salim YA, Hamidaddin MA, Yahya TA, Al-Ghorafi MA, Abdullah JH. Lisinopril-Excipient Compatibility Studies for Advanced Drug delivery Systems Development. World Journal of Pharmaceutical Research., 2024; 13(16): 59-111.
95. Saif AA, Alburyhi MM, Noman MA. Formulation and Evaluation of Ketoprofen Fast Dissolving Tablets. International Journal of Sciences., 2018; 7(09): 27- 39.
96. Al-Ghorafi MA, Alburyhi MM, Saif AA, Noman MA, Yahya TA. Drotaverine-Excipient Compatibility Studies for Advanced Drug delivery Systems Development. World Journal of Pharmaceutical Research., 2024; 13(18): 1285-1340.
97. Alburyhi MM, Noman MA, Saif AA, Hamidaddin MA, Yahya TA, Al-Ghorafi MA. Rosuvastatin-Excipient Compatibility Studies for Advanced Drug delivery Systems Development. World Journal of Pharmaceutical Research., 2024; 13(13): 1549-1582.
98. Alburyhi MM, Saif AA, Noman MA. Ticagrelor-Excipient Compatibility Studies for Advanced Drug delivery Systems Development. World Journal of Pharmacy and Pharmaceutical Sciences., 2024; 13(10): 1081-1132.
99. Alburyhi MM, Saif AA, Noman MA, Yassin SH. Simvastatin-Excipient Compatibility Studies for Advanced Drug delivery Systems Development. World Journal of Pharmaceutical Research., 2024; 13(19): 1463-1512.
100. Alburyhi MM, Saif AA, Noman MA, Al Khawlani MA. Bisoprolol -Excipient Compatibility Studies for Advanced Drug delivery Systems Development. World Journal of Pharmaceutical and Medical Research., 2024; 10(10): 304-324.
101. Alburyhi MM, Noman MA, Saif AA, Al-Ghorafi MA, Yahya TA, Yassin SH, Al Khawlani MA. Diclofenac-Excipient Compatibility Studies for Advanced Drug delivery Systems Development. World Journal of Pharmaceutical Research., 2024; 13(14): 1297-1333.
102. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of Aloe Vera Extract Capsules Delivery System as an Advanced Phytotherapy Approach for Controlling Diabetes. World Journal of Pharmacy and Pharmaceutical Sciences., 2024; 13(4): 1408-1423.
103. 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.
104. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of Curcuma Longa Extract Capsules Delivery System as an Advanced

Phytotherapy Approach for Cancer. European Journal of Biomedical and Pharmaceutical Sciences., 2024; 11(6): 37-43.
105. Alburyhi MM, Saif AA, Noman MA, Al Ghoury AA. Formulation and Evaluation of Antimalarial Drugs Suppositories. World Journal of Pharmaceutical Research., 2023; 12(20): 89-108.
106. 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.
107. 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.
108. Alburyhi MM, El-Shaibany A. Formulation and Evaluation of Antitumor Activity of Artemisia Arborescence Extract Capsules as Dietary Supplement Herbal Product Against Breast Cancer. World Journal of Pharmaceutical Research., 2024; 13(3): 95-114.
109. Alburyhi MM, Hamidaddin MA, Saif AA, Noman MA. Formulation and Evaluation of Rivaroxaban Orodispersible Tablets. World Journal of Pharmacy and Pharmaceutical Sciences., 2024; 13(2): 2066-2092.
110. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of Aloe Vera Extract Capsules Delivery System as an Advanced Phytotherapy Approach for Cancer. World Journal of Pharmaceutical Research., 2024; 13(8): 1052-1072.
111. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of Aloe Rubroviolaceae Extract Capsules Delivery System as an Advanced Phytotherapy Approach for Hepatoprotective. European Journal of Biomedical and Pharmaceutical Sciences., 2024; 11(4): 53-61.
112. 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.
113. Noman MA, Alburyhi MM, El-Shaibany A, Alwesabi NA. Preformulation and Characterization Studies of Pandanus Odoratissimus L Extract Active Ingredient in Treatment of Nocturnal Enuresis. World Journal of Pharmacy and Pharmaceutical Sciences., 2024; 13(2): 1603-1620.
114. Alburyhi MM, El-Shaibany A. Formulation and Evaluation of Antibacterial Orodispersible Tablets of Artemisia Arborescence Extract Herbal Product. European Journal of Pharmaceutical and Medical Research., 2024; 11(2): 409-417.
115. Alburyhi MM, Saif AA, Noman MA, Yassin SH. Formulation and Evaluation of Simvastatin Orodispersible Tablets. World Journal of Pharmaceutical Research., 2023; 12(16): 1033-1047.
116. 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.
117. 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.
118. 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.
119. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of Dictyota Dichotoma Extract Medicinal Seaweed Capsules Delivery System as an Advanced Phytotherapy Approach for Cancer. European Journal of Biomedical and Pharmaceutical Sciences., 2024; 11(4): 63-70.
120. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of Celery Extract Capsules Delivery System as an Advanced Phytotherapy Approach for Gout. World Journal of Pharmaceutical Research., 2024; 13(11): 2383-2404.
121. Raweh SM, Noman MA, Alburyhi MM, Saif AA. Formulation and Evaluation of Anti-acne Gel of Azadirachta Indica Extract Herbal Product. European Journal of Pharmaceutical and Medical Research, 2024; 11(2): 427-433.
122. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of Acalypha Fruticosa Extract Tablets Delivery System as an Advanced Phytotherapy Approach for Controlling Diabetes. World Journal of Pharmaceutical Research., 2024; 13(8): 1073-1091.
123. Noman MA, Alburyhi MM, Alqubati MA. Preformulation and Characterization Studies of Clopidogrel Active Ingredient for Orodispersible Tablets Development. World Journal of Pharmacy and Pharmaceutical Sciences., 2024; 13(3): 996-1015.
124. Alburyhi MM, Saif AA, Noman MA. Formulation and Evaluation of Ticagrelor Orodispersible Tablets. World Journal of Pharmaceutical Research., 2024; 13(5): 26-55.
125. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of Tribulus Terrestris Extract Capsules Delivery System as an Advanced Phytotherapy Approach for Kidney Stones. World Journal of Pharmacy and Pharmaceutical Sciences., 2024; 13(5): 1425-1443.
126. 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.
127. 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.
128. Alburyhi MM, Saif AA, Saif RM. Preformulation Study of Ceftriaxone and Ciprofloxacin for Lipid Based Drug Delivery Systems. EJUA-BA, 2022; 3(4): 339-350.
129. Alburyhi MM, Noman MA, Saif AA. Formulation and Evaluation of Natural Herbal Anti-acne as Gel Delivery Systems. World Journal of Pharmaceutical Research., 2024; 13(21): 1447-1467.
130. Alburyhi MM, Salim YA, Saif AA, Noman MA. Furosemide-Excipient Compatibility Studies for Advanced Drug delivery Systems Development. World Journal of Pharmaceutical Research., 2024; 13(22): 1178-1219.
131. Alburyhi MM, Salim YA, Saif AA, Noman MA. Amlodipine-Excipient Compatibility Studies for Advanced Drug delivery Systems Development. World Journal of Pharmacy and Pharmaceutical Sciences., 2024; 13(11): 95-136.
132. Noman MA, Alburyhi MM, Saif AA, Yahya TAA. Evaluation and Drug Stability Studies Some Atorvastatin Tablets Brands Available in Sana'a Market Yemen. World Journal of Pharmaceutical and Medical Research., 2024; 10(12): 231-236.
133. Alburyhi MM, Noman MA, Alemad AF. Preformulation Studies of Cefixime for Dispersible Tablets Delivery System Development. World Journal of Pharmacy and Pharmaceutical Sciences., 2024; 13(12): 75-99.
134. Al-Ghorafi MA, Alburyhi MM, Muthanna MS. Chemical Incompatibilities of IV Admixture Combinations in ICU, Orthopedic and Emergency Units of Various Hospitals and Medical Centers in Sana'a, Yemen. European Journal of Pharmaceutical and Medical Research., 2023; 10(10): 416-425.
135. Salim YA, Yahya TA, Hamidaddin MA, Alburyhi MM. An In-Vitro New Bioequivalence Study and Densitometric Method for Determination of Azithromycin Tablets of Different Brands. Asian Journal of Pharmaceutical Analysis and Medicinal Chemistry., 2020; 8(4): 147-152.
136. Noman MA, Alburyhi MM, Saif AA, Yahya TAA. Formulation and Evaluation of Polyherbal Extract for Skin Hyperpigmentation as Gel Advanced Delivery Systems. World Journal of Pharmaceutical Research., 2024; 13(22): 1260-1280.
137. Saif AA, Noman MA, Alburyhi MM, Yahya TAA. Evaluation and Drug Stability Studies Some Levocetirizine Tablets Brands Available in Sana'a Market Yemen. World Journal of Pharmaceutical Research., 2024; 13(24): 1009-1022.
138. Alburyhi MM, Noman MA, AA Saif. Formulation and Evaluation of Meloxicam Emulgel Delivery System for Topical Applications. World Journal of Pharmaceutical Research., 2025; 14(4): 1324-1337.
139. Alburyhi MM, El-Shaibany A, Al-Wajih AM, Alqadhi AA, Almlhani AN. Advancements in Nano-Formulation Systems for Enhancing the Delivery of Herbal Ingredients. European Journal of Pharmaceutical and Medical Research., 2025; 12(1): 212-231.
140. Al-Ghorafi MA, Alburyhi MM, Muthanna MS. Effect of Rosemary and Myrtus Extracts Combination on Androgenetic Alopecia: A Comparative Study with Minoxidil. European Journal of Pharmaceutical and Medical Research., 2023; 10(10): 35-39.
141. Alburyhi MM, Noman MA, Saif AA, Alemad AF. Dispersible and Orodispersible Tablets Delivery Systems for Antibacterials Development. World Journal of Pharmaceutical Research., 2025; 14(1): 1229-1257.
142. Alburyhi MM, El-Shaibany A, Al-Wajih AM, Almlhani AN, Alqadhi AA. Innovative Approaches in Herbal Drug Delivery Systems Enhancing Efficacy and Reducing Side Effects. World Journal of Pharmacy and Pharmaceutical Sciences., 2025; 14(1): 919-929.
143. 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.
144. Al-Ghorafi MA, Alburyhi MM, Saif AA, Noman MA. Meloxicam-Excipient Compatibility Studies for Advanced Drug delivery Systems Development. World Journal of Pharmaceutical and Medical Research., 2025; 11(1): 87-106.
145. Alburyhi MM, Saif AA, Noman MA. Domperidone-Excipient Compatibility Studies for Advanced Drug delivery Systems Development. World Journal of Biomedical and Pharmaceutical Sciences., 2025; 12(3): 250-269.
146. Alburyhi MM, Saif AA, Noman MA. Spironolactone-Excipient Compatibility Studies for Advanced Drug delivery Systems Development. World Journal of Pharmacy and Pharmaceutical Sciences., 2025; 14(3): 871-910.
147. Alburyhi MM, Saif AA, Noman MA. Clopidogrel-Excipient Compatibility Studies for Advanced Drug delivery Systems Development. World Journal of Pharmaceutical Research., 2025; 14(6): 1448-1486.
148. Graham PH, Browne L, Cox H, Graham J. Inhalation aromatherapy during radiotherapy: results of a placebo-controlled double-blind randomized trial. J Clin Oncol., 2003; 21: 2372–2376.
149. Hadfield N. The role of aromatherapy massage in reducing anxiety in patients with malignant brain tumours. Int J Palliat Nurs., 2001; 7: 279–285.
150. Subiza J, Subiza JL, Alonso M, Hinojosa M, Garcia R, Jerez M, Subiza E. Allergic conjunctivitis to chamomile tea. Ann Allergy., 1990; 65: 127–132.
151. Gupta V, Mittal P, Bansal P, Khokra SL, Kaushik D.

Pharmacological potential of Matricaria recutita-a review. In- ternational Journal of Pharmaceutical Sciences and Drug Research., 2010; 2(1): 12–16.
152. Chauhan ES, Jaya A. Chamomile an Ancient Aromatic Plant - A Review. Journal of Ayurveda Medical Sciences., 2017; 2(4): 251-5.