

## FORMULATION, DEVELOPMENT AND EVALUATION OF CAPSICUM EXTRACT CAPSULES DELIVERY SYSTEM AS AN ADVANCED PHYTOTHERAPY APPROACH FOR TONIC AND NATURAL STIMULANT ACTIONS

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### ABSTRACT

*Capsicum*, commonly known as Chili peppers, has a long history of Medicinal properties, primarily as a digestive, thermogenic, carminative, stimulant, cardiogenic, antipyretic, sordorific, rubefacient & sialagogue. *Capsicum annuum* is the most widely cultivated and distributed species in Yemen. Paprika, *Capsicum annuum* L. (Solanaceae) is one of the oldest, most important and widely used carotenoid food colorants. *Capsicum* is a remarkable whole-body stimulant that can boost blood flow, tone the nervous system, relieve indigestion, promote sweating, help to cauterize and heal ulcers, ease persistent pain and fight off infection. Because *Capsicum* boosts peripheral circulation and stimulates organ secretion, it expedites the therapeutic delivery and action of other herbs. *Capsicum* stimulates everything from blood flow to peristaltic action in the stomach, to intestinal transit time. The remarkable ability of *Capsicum* to stimulate organ secretion and even heart action makes it one of the strongest natural stimulants known. Several different kinds of herbal blends targeting various body systems will utilize *Capsicum* to boost the formulations efficacy. A *Capsicum* was formulated as capsules and evaluated for organoleptic properties and other evaluation parameters. It was concluded that among the all formulations of *Capsicum* extract capsules the F1 was found to be as an optimized capsules according to drug release percentage 90% within 60 minutes, so the F1 was the best formulation of *Capsicum* extract capsules delivery system as an advanced phytotherapy approach for tonic and stimulant actions.

**KEYWORDS:** *Capsicum*, Extract, Capsules, Tonic, Natural Stimulant actions.

### INTRODUCTION

#### **Capsicum**<sup>[1-79]</sup>

Chili is known by different names in different parts of the world. The genus *Capsicum*, which is commonly known as "red chili", "chili pepper", "hot red pepper", "tabasco", "paprika", "cayenne", etc., belongs to the family *Solanaceae*. The original distribution of this species appears to have been from the south of Mexico, extending into Columbia. The taxonomy of the genus *Capsicum* is confounded within certain species complexes. It is generally believed that about 20 *Capsicum* species are distributed worldwide. The five major species of *Capsicum* cultivated are: *Capsicum annuum*, *Capsicum frutescens*, *Capsicum Chinese*, *Capsicum pendulum* and *Capsicum pubescens*. *Capsicum annuum* is the most widely cultivated and distributed species in Yemen.

Paprika, *Capsicum annuum* L. (*Solanaceae*) is one of the oldest, most important and widely used carotenoid food colorants. *Capsicum*, commonly known as *Chili peppers*, has a long history of Medicinal properties, primarily as a digestive, thermogenic, carminative, stimulant, cardiogenic, antipyretic, sordorific, rubefacient & sialagogue. More often than not, most of us regard red pepper or *Capsicum* or cayenne as nothing more than the spice added to give Cajun and Mexican cuisine its piquant kick. Technically speaking, cayenne pepper is the strongest red pepper variety of the *Capsicum* family, with paprika being the mildest. Health practitioners have known for centuries that *Capsicum* is much more than a culinary spice. Because they considered it a "hot" plant, Chinese physicians utilized it for physiologic conditions that needed stimulation. *Capsicum* or *Cayenne Pepper* is one of the few herbs that can be measured by its BTU or thermal units. In other words, it is a hot and stimulating

pepper plant that can generate heat.

Recently, new and very valuable medicinal uses for *Capsicum* have emerged through scientific inquiry. The red chili pepper is experiencing a rediscovery among health care practitioners, who have only just begun to uncover its marvelous therapeutic actions.

It has been referred to as the purest and most effective natural stimulating botanical in the herbal medicine chest. The most recent clinical findings regarding *Capsicum* will be explored on *Capsicum*'s ability to heal ulcers, protect stomach mucosa and alleviate peripheral pain.

*Capsicum* exerts potent physiological and pharmacological effects without the side effects commonly associated with powerful medicinal drugs. Ironically, in the past, *Capsicum*'s classification as a hot and spicy substance has done it a disservice. Because *Capsicum* is fiery and pungent, it is frequently regarded as dangerous and unpalatable. To the contrary, if it is used properly, *Capsicum* can be perfectly safe and impressively effective against a wide variety of physical disorders ranging from indigestion to ulcers to migraines. Its ability to lower blood cholesterol, boost circulation and even step-up metabolism are worth serious consideration. In a time when the notion of treating disease after the fact is more the rule than the exception, *Capsicum* offers protection from infectious invaders by boosting the effectiveness of the immune system. Today, amidst the over prescription of antibiotic drugs, *Capsicum* emerges as a potent immune fortifier, antioxidant and infection fighter.

A powerful compound called capsaicin is what gives *Capsicum* its bite and is also responsible for most of its beneficial effects on human physiology. The hotter the pepper, the higher its content of capsaicin the remarkable properties of capsaicin. It is important to realize in evaluating this herb that while it can be used alone, *Capsicum* is frequently added to herbal combinations to potentiate their overall action. This fact alone attests to the powerful but safe stimulant action of *Capsicum*. Stimulation is thought to be one of the keys to swift and complete healing. *Capsicum* is ascending in prestige and is regarded as a modern-day botanical, which is accruing new and impressive credentials. The fruit of this particular pepper plant is a valuable herbal treasure. It is vital to our health that we inform ourselves about its many medicinal uses.

#### Historical and Popular Uses

Once an official medicine in the United States, *Capsicum* was an official drug listed in both the U.S. Pharmacopoeia and the National Formulary into the 1950s. It was listed as a carminative (relieves gas), stimulant, and rubefacient (used as a counterirritant for muscle pain). *Cayenne* is still an official drug in Germany approved in the Commission E monographs.

Traditionally *Cayenne* has been used for its stimulant actions, especially with respect to the circulatory and digestive systems. It is said to increase blood flow thus allaying peripheral vascular disorders, decrease blood pressure, tonify the nervous system, increase appetite, relieve indigestion, and act as a carminative (relieves gas and flatulence). It has antiseptic and antibacterial properties and has made for an excellent gargle for sore throats. *Cayenne* can be useful as a diaphoretic (a sweat inducing herb), especially when used with Yarrow.

Old timers used it at the first onset of a cold, when a chill was coming on, or to break a fever. The Chinese believe *Cayenne* stimulates yang, the masculine active principle in nature that is exhibited in light, heat, or dryness and that combines with yin to produce harmony in the body. They also believe, as do most herbalists, that *Cayenne* is an accentuator of other herbs, increasing the value and healing properties of other herbs in a formula by carrying them to afflicted parts of the body via its ability to stimulate circulation. *Cayenne* or *Capsicum* gets its name for the Greek kaptos, meaning I bite (no leap of faith here). The origin of the species is buried in antiquity, but experts believe that all of the varieties of chilies came from one species. Perhaps this is why sometimes *Cayenne* is described as being derived from *C. annuum*, and sometimes from *C. frutescens*, and other times from a mixture. For this reason, it makes more sense to judge a *Capsicum* medicine by the active to which it is standardized and its heat units value.

**Modern Day Uses:** Topical post-herpetic neuralgia: the pain associated with shingles. Post-surgical pain: including postmastectomy and post amputation. Diabetic neuropathy: sensations of pain, temperature, and pressure, especially in the lower legs and feet. Arthritis: both rheumatoid and osteo. Various other neuropathic and complex.

Oral Stimulant to the digestive system. Circulation and high blood pressure. High cholesterol reduces blood clotting tendencies by reducing platelet aggregation and increasing fibrinolytic activity prevention or arteriosclerosis and heart disease, prevention of GI damage when taken ½ hour before aspirin.

The peppers were a wonderful source of essential vitamins in a diet otherwise lacking in them. *Capsicum* continues to be a source of vitality and health in numerous countries including the Bahamas and Costa Rica, where it is used to overcome colic or indigestion, in Africa for vascular disorders and by North Americans who use it as a tonic and natural stimulant. *Capsicum* is currently experiencing a renaissance in that a number of recent studies have emerged adding to its already impressive list of actions. Scientists are taking notice and looking at *Capsicum* with new respect and interest. Perhaps what sets *Capsicum* apart is that unlike powerful pharmaceutical stimulants and painkillers, *Capsicum* possess potency without deleterious side effects.

**Active Chemical Constituents:** Alkaloids (capsaicin), fatty acids, flavonoids, volatile oil and carotene pigment. The nutritional breakdown of *Capsicum* is as follows: Fats: 9-17%, Proteins:12-15%, Vitamin A and red carotenoids (capsanthin, carotene, lutein), Ascorbic Acid (Vitamin C), B-Complex vitamins, Potassium: 2014 mg per 100 edible grams, Rutin (flavonoid) and PABA.

Note: *Capsicum*'s red color is due in part to its very high content of vitamin A, which is vital for normal vision, cellular activity, growth and strong immune defenses.

#### Pharmacological Activities of *Capsicum*

Capsaicin (active component) contains over 100 distinct volatile compounds. It also contains capsaicin, capsaicin, capsaicin. It has action: Analgesic, Antioxidant, Antipyretic, Antibacterial, Antiseptic, Antispasmodic, Carminative, Astringent, Blood thinners, Cardiovascular tonic, Circulatory stimulant, Diaphoretic, Emostatic, Nerve stimulant stomachic and tonic (general).

Body Systems Targeted: Cardiovascular, circulatory, gastrointestinal, nervous, integumentary, skeletal and metabolic.

#### Products and Uses

*Capsicum* is a remarkable whole-body stimulant that can

boost blood flow, tone the nervous system, relieve indigestion, promote sweating, help to cauterize and heal ulcers, ease persistent pain and fight off infection. One very authoritative work on African plants suggests that *Capsicum*'s "regular ingestion is highly beneficial in hemorrhoids, varicose veins, anorexia, liver congestion and vascular conditions. The indigenous inhabitants of Africa and of the Antilles are remarkably free from all of these conditions as they use *Capsicum* fruit in their diet". Most of the therapeutic actions of *Capsicum* are attributed to the alkaloid or glucoside content of the herb. The latest scientific studies conducted with *Capsicum* will be discussed in subsequent sections.

*Capsicum* can be used liberally in a variety of forms. Capsulized dried *Capsicum* is probably the easiest and most practical way to take the herb. Commercial ointments can be purchased which contain from 0.025 to 0.075 percent capsaicin for the treatment of pain and psoriasis. Dried powder *Capsicum* can be mixed in hot water or can be used in tincture form, which can be added to water or juice, infused oil and cream.

The *Capsicum* family *Capsicum annum L.* (*Solanaceae*), which is a member of *Capsicum*, has several species that are known for their tonic and stimulant properties. As shown in Figure1.



Fig. 1: *Capsicum Annuum L.* (*Solanaceae*).

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).

#### Herbal Catalyst

Because *Capsicum* boosts peripheral circulation and stimulates organ secretion, it expedites the therapeutic delivery and action of other herbs. In other words, the medicinal benefits of these herbs reach infected or inflamed tissue more rapidly due to enhanced blood flow. Consider the following statement: *Cayenne* will insure the rapid and even distribution of the active principles of the rest of the herbs to critical functional centers of the body, including those involved in cellular respiration, metabolism, data transmission, and neural-hormonal activation. *Cayenne* is included in several other blends for this reason. In extremely small quantities it can dramatically increase the efficiency of most other

herbs. Many health practitioners believe that the key to healing is stimulation. *Capsicum* stimulates everything from blood flow to peristaltic action in the stomach, to intestinal transit time. The remarkable ability of *Capsicum* to stimulate organ secretion and even heart action makes it one of the strongest natural stimulants known. Several different kinds of herbal blends targeting various body systems will utilize *Capsicum* to boost the formulations efficacy.

#### Toxicity and Contraindications

*Capsicum* is generally recognized as safe in the United States and has been approved as an over-the-counter drug. Safety during pregnancy and breast feeding. Pregnant women or breast-feeding mothers should avoid using *Capsicum*. Initial use of topical *Capsicum* can result in some skin irritation or burning; however, clinical tests have found that this diminishes with continued application. Avoid direct contact with eyes or other mucous membranes in general.

### The Capsule Delivery System<sup>[80-175]</sup>

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 *Capsicum* extract powder solid dosage form of *Capsicum* capsules delivery system was prepared and evaluated as an advanced phytotherapy approach for tonic and natural stimulant actions.

### MATERIALS AND METHODS

The extract of *Capsicum* 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 (0.1N HCl), 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 *Capsicum* Extract<sup>[80-175]</sup>

#### 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 *Capsicum* 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
<b>Very Soluble</b>	Less than 1
<b>Freely Soluble</b>	From 1 to 10
<b>Soluble</b>	From 10 to 30
<b>Sparingly Soluble</b>	From 30 to 100
<b>Slightly Soluble</b>	From 100 to 1000
<b>Very slightly Soluble</b>	From 1000 to 10,000
<b>Practically Insoluble</b>	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:

$$\text{Bulk density} = \text{Bulk Mass} / \text{Bulk Volume}$$

#### Carr's compressibility index

$$\text{Carr's index (\%)} = (\text{Tapped density} - \text{Poured density}) / \text{Tapped density}$$

**Table 2: Carr's Index of Powder Flowability.**

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

#### Formulation of *Capsicum* Extract Capsules

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



**Table 3: Formulation of *Capsicum* Extract Capsules.**

Ingredients	Quantity Per Capsule (mg)		
	Formulation Code		
	F1	F2	F3
<b><i>Capsicum</i> Extract</b>	10%	10%	10%
<b>Diluent I</b>	49%	59%	30%
<b>Diluent II</b>	40%	30%	59%
<b>Lubricant</b>	1%	1%	1%

### Evaluation of *Capsicum* Extract Capsules

#### Determination of Uniformity of Weight and The Amount of *Capsicum* Capsules

For the determination of the uniformity of weight, the British Pharmacopoeia method was used. In which Twenty of the *Capsicum* 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, 10% of *Capsicum* 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 *Capsicum* 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 *Capsicum* 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 281nm, the wavelengths for maximum UV absorbance of solutions of the *Capsicum* 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:  $37 \pm 0.5^\circ\text{C}$ . 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  $37 \pm 0.5^\circ\text{C}$  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 *Capsicum* Extract

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

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

Properties	<i>Capsicum</i> Extract
<b>Physical Appearance</b>	Small Powder
<b>Color</b>	Red
<b>Odor</b>	Aromatic and Penetrating Odor
<b>Taste</b>	Spicy, Pungent, Hot and Biting

The *Capsicum*, spicy, pungent, hot and biting taste, aromatic and penetrating odor, and red color, 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 *Capsicum* 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 *Capsicum* extract show that the extract is sparingly soluble in water as shown in Table 5.

**Table 5: Evaluation Parameters of *Capsicum* Extract.**

Testing	<i>Capsicum</i>
The Solubility of Extract	Sparingly Soluble in Water
Carr's Index (%)	12%
Particle Size	Coarse Powder
The Moisture Content (%)	2%

**The Flowability of Extract**

The Carr's index of compressibility for *Capsicum* extract is 12% show that the *Capsicum* 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 *Capsicum* Extract Capsules**

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

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

The average deviation in weight from average for *Capsicum* capsules were found to be 0.80% and average total content per capsule was 100%, within the limit on the acceptable deviation in weight from average for capsules therefore, mentioned results thus indicated that the *Capsicum* capsules are within the limit of the British Pharmacopoeia specifications.

**In-Vitro Dissolution Studies of *Capsicum* Extract Capsules****Table 6: The Drug Release Percentage of *Capsicum* Extract Capsules.**

Drug Release %				
Formulation Code				
		F1	F2	F3
Time (min)	15	80	32	23
	30	84	53	44
	45	85	68	61
	60	90	82	74

The *in-vitro* dissolution percentage of *Capsicum* extract capsules is one important of the results of dissolved active ingredient, *Capsicum* extract, as shown in Table 6. The results of formulation have shown that the drug release of F1 was found to be 84% within 30 minutes in buffer medium. The results of formulation have shown that the drug release of F1 was found to be 85% within 45 minutes in buffer medium. The results of formulation have shown that the drug release of F1 was found to be 90% within 60 minutes in buffer medium.

**CONCLUSION**

*Capsicum* is a remarkable whole-body stimulant that can boost blood flow, tone the nervous system, relieve indigestion, promote sweating, help to cauterize and heal ulcers, ease persistent pain and fight off infection. It was

concluded that among the all formulations of *Capsicum* extract capsules the F1 was found to be as an optimized capsules according to drug release percentage 90% within 60 minutes, so the F1 was the best formulation of *Capsicum* extract capsules delivery system as an advanced phytotherapy approach for tonic and natural stimulant actions.

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