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Theme

Formulation of a syrup and tablets based on *Asparagus officinalis* has an anti-inflammatory effect

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Abstract

The present study examines the development of two galenic forms from *Asparagus officinalis*: a syrup and tablets. *Asparagus officinalis* is a medicinal plant known for its diuretic, anti-inflammatory, antioxidant, and immunomodulatory properties, attributed to its bioactive components such as saponins, flavonoids, and phenolic acids. The choice of syrup is motivated by its ease of administration, particularly for children and the elderly, while tablets offer increased convenience and stability. The objective is to create effective and stable formulations that preserve the pharmacological properties of the plant. The methodology includes the extraction of active ingredients, product formulation, and evaluation of their stability and efficacy. The preparation of the syrup and tablets involves steps of maceration and vacuum evaporation to extract the active substances, followed by rheology, pH, and compressibility tests to ensure quality and compliance with pharmaceutical standards.

Keys Word: *Asparagus officinalis***,** Extraction, Formulation**,** syrup and tablets

Résumé

Le présent travail examine le développement de deux formes galéniques à partir d'Asparagus *officinalis* : un sirop et des comprimés. *Asparagus officinalis* est une plante médicinale connue pour ses propriétés diurétiques, anti-inflammatoires, antioxydantes et immunomodulatrices, attribuées à ses composants bioactifs tels que les saponines, flavonoïdes et acides phénoliques. Le choix du sirop est motivé par sa facilité d'administration, particulièrement pour les enfants et les personnes âgées, tandis que les comprimés offrent une commodité et une stabilité accrues. L'objectif est de créer des formulations efficaces et stables qui préservent les propriétés pharmacologiques de la plante. La méthodologie comprend l'extraction des ingrédients actifs, la formulation des produits et l'évaluation de leur stabilité et efficacité. La préparation du sirop et des comprimés implique des étapes de macération et d'évaporation sous vide pour extraire les substances actives, suivies de tests de rhéologie, de pH, et de compressibilité pour assurer la qualité et la conformité aux normes pharmaceutiques.

Mots clés : *Asparagus officinalis***,** Extraction, Formulation**,** sirop et comprimés

الملخص

تبحث هذه الدراسة في تطوير شكلين غالينيين من نبات الهليون المخزني : شراب وأقراص .يعتبر نبات الهليون المخزني نبات طبي معروف بخصائصه المدرة للبول والمضادة للالتهابات والمضادة للأكسدة والمعدلة للمناعة، والتي تعزى إلى مكوناته النشطة بيولوجيًا مثل الصابونين والفلافونويد والأحماض الفينولية .الدافع وراء اختيار الشراب هو سهولة تناوله، خاصةً للأطفال وكبار السن، بينما توفر الأقراص راحة وثباتاً أكبر .والهدف من ذلك هو إنشاء تركيبات فعالة ومستقرة تحافظ على الخصائص الدوائية للنبات .تتضمن المنهجية استخلاص المكونات النشطة وصياغة المنتجات وتقييم ثباتها وفعاليتها . ويتضمن تحضير الشراب والأقراص مراحل النقع والتبخير بالتفريغ لاستخلاص المواد الفعالة، تليها اختبارات الريولوجيا و الحموضة وقابلية الانضغاط لضمان الجودة والامتثال للمعايير الصيدلانية.

الكلمات المفتاحية : الهليون المخزني، الاستخلاص، التركيب، الشراب والأقراص.

ACKNOWLEDGEMENT AND DEDICATION

First of all, we would like to thank our Lord for giving us health and courage until the end of our studies and the completion of this work.

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We dedicate this modest work to our very dear parents, who really supported us, for their efforts and sacrifices, for their advice and wisdom.

We also dedicate this work to our paternal and maternal grandparents; may God protect them.

Not forgetting our brothers and sisters and all our cousins, not forgetting our friends and companions in the same field during my university career.

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ABBREVIATIONS LIST

IC : Carr index

IH : Haussner index

Mg : Magnesium

V-bulk : Bulk volume

V-tapped : Tapped volume

F: Friability

AI : Active ingredient

UV : Ultra-violet

ABSn : Absorbency of each batch

Abs max : Maximum absorbency

V: Volume

N: Newton

Mm : Millimeters

SUMMARY

GENERAL INTRODUCTION

Since the dawn of humanity, a multitude of plants native to the surrounding environment have been employed to treat and cure a plethora of ailments. These plants represent a vast reservoir of potential compounds linked to secondary metabolic processes, which have the advantage of having a wide variety of chemical structures and a wide range of biological activities.

Nevertheless, the assessment of these activities represents a fascinating subject that could be the subject of numerous studies. In the ongoing battle against microbial diseases, antibiotics have been regarded as the ultimate weapon. Nevertheless, the phenomenon of antibiotic resistance in several species and genera, as well as the unexpected side effects of synthetic drugs, have brought phytophilia back to the public eye **(Mazari et *al.*, 2010).**

Due to their unique biological properties, which are primarily characterized by their antioxidant and antimicrobial effects, medicinal plants are extensively employed in traditional medicine to treat a diverse range of diseases and infections **(Hennebelle et *al.*, 2004).**

In addition to their use as food, plants also possess medicinal benefits that allow them to be used in the treatment of a variety of diseases. Consequently, an assessment of the potential importance of these plants can assist in clarifying the medicinal value of these plants **(Pandey et *al.*, 2006).**

In light of the aforementioned considerations, a considerable body of research has been conducted in recent years on medicinal or edible plants with the objective of identifying compounds exhibiting antioxidant properties that can protect against a range of diseases **(Kindl et *al.*, 2015).**

The development of chemical analysis techniques has demonstrated that a plant species is capable of synthesizing thousands of distinct chemical components, which are categorized into two main groups: primary and secondary metabolisms. The original chemical profile of each plant species is characterized by a secondary metabolism, which is shaped by time and evolution and results in a high degree of molecular biodiversity (**Wichtel et *al.*, 1999).**

The use of *Asparagus officinalis* in the fields of nutrition and medicine is an area of interest to those studying the species. Aspartame represents an invaluable source of essential nutrients .

Vital compounds and oligosaccharides **(Fukushi et *al.*, 2000).** Furthermore, these plants contain flavonoids (principally rutin) and phenolic compounds, which possess potent antioxidant propertie **(Makris et *al.*, 2001).**

To this end, we will first review some basic knowledge of the Medicinal Plants, general information on *Asparagus officinalis*, and Current extraction and formulations techniques. Then, in the experimental section, we'll look at the development of two galenic forms from *Asparagus officinalis*: a syrup and tablets. Finally, a discussion of the results will be followed by a conclusion and perspectives

1. Medicinal Plants

1.1. General information's about medicinal plants

Definition of a medicinal plant is relatively straightforward. Indeed, it is a plant that is employed to prevent, treat, or soothe a multitude of ailments. These are plant substances that exhibit at least some medicinal properties **(Farnsworth et *al*., 1986).**

According to **Debuigne et *al*., (2009),** A medicinal plant is defined as a plant that has a therapeutic effect on the body when administered in a normal dose, without causing toxicity. Traditional knowledge of effects of medicinal plants is well established, but ttherapeutic properties of individual plant parts may vary **(Colette, 2004).**

Traditional pharmacopoeia employs the use of different plant parts as chemical plants, which are capable of generating naturally occurring, biologically active substances. Harvesting of plants is contingent upon the attainment of mmaximum number of active substances **(Schauenberg et *al*., 2012).**

According to Chabrier (2010), Plant parts employed include roots, crusts, flower tops, leaves, flowers, fruits and seeds. These components may be preserved in their entirety or in a fragmented state, and in certain instances, entire plant may be utilized.

Chabrier (2010), indicate that plant material employed includes roots, crusts, flower tops, leaves, flowers, fruits and seeds. These components can be preserved in their entirety or as fragmented elements, and in certain instances, entire plant may be utilized. Consequently, approximately 80% of global population utilises traditional medicine as a primary source of healthcare **(WHO, 2002)**. According to **Sheng (2001),** It is estimated that more than half of world's population relies on medicinal plants as a primary form of self-treatment.

According to **Farnsworth and Soejarto (1991),** Medicinal plants are employed in production of pharmaceuticals, including teas, ointments, creams, and other natural products. As indicated by **Farnsworth and Soejarto (1991),** approximately 90 species are employed in production of most significant industrial pharmaceuticals, it is common practice in developing countries to utilise traditional remedies that are derived from a combination of herbs gathered from the wild. It can be observed that active substances in question are derived primarily from plants, and not only in context of traditional medicine.

1.1.1. Apercus on Asparagus officinalis

Asparagus officinalis L. is a species of plant belonging to the family Asparagaceae. Asparagus plants are dioecious, perennial, and dichogamous. Asparagus is cultivated for its juvenile stems, known as turions, which emerge from soil in spring and are harvested on a daily basis for approximately two months. In winter, the plant enters a period of dormancy, except in warm climates where it continues to grow throughout the year **(Doré, 1990).**

1.1.2. Taxonomy of Asparagus officinalis

Taxonomy of Asparagus officinalis, is given according to Al Snafi (2013) in the following tables first cultivated asparagus in 200 BC, then the Romans (Elena, 2007).

Table I: Taxonomy of A*sparagus officinalis*

Taxonomic Rank	**Scientific Name**
Kingdom	Plantae
Division	Tracheophyta
Subdivision	Spermatophyta
Class	Magnoliopsida
Order	Asparagales
Family	Asparagaceae
Subfamily	Asparagoideae
Tribe	Asparageae
Genus	*Asparagus*
Species	*Asparagus officinalis L.*

1.1.3. Botanical and systematic description

It is an herbaceous perennial plant. With short joints, rampant handle holder, thick, tuberously swollen. Size: between 60 and 150 cm. The verticils have multiple branching stems, with 2 to 6 needle-shaped stems. Flower: Common (actinomorphic), of a white-greenish yellow, 4 to 6 mm wide, with 6 lobes, fused. Male flowers are narrowly campanulated, while the female and bisexual are almost oval.

A unique style of fused gynoecium. Solitary or pairs of flowers - a few verticillary flowers at the ends of the leaves. Leaves: rudimentary scales. Axillary needle-shaped stems, verticillated. Ripe orange has a round fruit, initially green, measuring from 6 to 10 mm (0.24 to 0.4 in) wide **(Anonyme, 2012 ; Grubben, 2004).**

Figure 1: Morphology of the *Asparagus* plant

1. Asparagus turion; 2. Asperger leaf; 3. Asperge crown with fleshy buds and roots; 4. Asparagus flower; 5. Vertical cutting of the asparagus flower; 6. Vertical Cutting of one asperge seed; 7. Ovary; 8. Vertical cut of the ovaries; 9. Asparagus fruit. (Anonym, 2017)

1.1.4. Geographical distribution of Asparagus officinalis

Plant has been distributed in Central and Southern Europe, the Middle East, Western Siberia and North Africa. It has been grown in many places. It was distributed in: Algeria, Morocco, Tunisia (Africa); Afghanistan, Iran, Iraq, Lebanon, Syria, Turkey, Armenia, Azerbaijan, Georgia, Russian Federation, Kazakhstan, Mongolia and China (Asia); Denmark, Austria, Belgium, Czech Lovaquie, Germany, Hungary, Netherlands, Poland, Switzerland, Belarus, Moldova, Ukraine, Albania, Bulgaria, former Yugoslavia, Greece, Italy, Romania, France, Portugal, Spain, Finland, Norway, Sweden, Estonia, Latvia and Lithuania (Europe);

United States and Cana da (Bolivarian, Ecuadorian, Argentine and Uruguay (South America); as well as Australia and New Zealand **(Anonyme, 2012)**

1.1.5. Major active substances of asparagus

Medicinal plants contain active ingredients, which are referred to as active substances. Therapeutic qualities of medicinal plants vary considerably between species. Each individual plays a specific role within the ecosystem (**EL ABED et *al*.,2007).**

According to **Cheriti et *al*. (2007),** uutilisation of traditional medicine plants offers significant potential in both the medical and economic realms, as they provide the essential raw materials for production of medicines. According to **EL ABED et *al*., (2007),** active compounds of medicinal plants are primarily comprised of three chemical groups: polyphenols, alkaloids and essential oils.

Asparagus officinalis contains a variety of steroid saponins, including asparagus A, B, D, F, G, H, I, bitter steroid saponins, amino acids, fructans (asparagose and asparagosin), ferulic acid, minerals, vitamins, and flavonoids. It has been demonstrated to possess anti-cancer, antimicrobial, antioxidant, hypolipidemic, anti-diabetic, and numerous other properties. According to **Al Snafi (2015),** this article will highlight the chemical components and pharmacological properties of Asparagus officinalis. Main constituents of asparagus are:

- **Flavonoids**

Flavonoids constitute a set of more than 6000 natural compounds that are almost universally present in vascular plants. These pigments are responsible for the yellow, orange and red shades observed in various plant organs. Furthermore, flavonoids are present in a number of medicinal plants. Flavonoids have been employed in traditional medicine worldwide, with herbal remedies containing these compounds being used in various cultures. According to GHEDIRA (2005), All flavonoids are derived from the benzo-γ-pyrone chain and can be structured according to the nature of various substitutes present on the molecular cycles, as well as the degree of saturation of the benzopyrone skeleton.

- **Tannins**

Polyphenol polymers with high molecular weight, commonly referred to as tanins, have capacity to precipitate a range of substances, including alkaloids, gelatin, and other proteins. In addition to their classical properties, tanins exhibit a unique ability to precipitate these substances. These bodies are employed in the tanning industry due to their capacity to transform

fresh animal skins into leather (RIBEREAU-GAYON, 1968). Hydrolysable and condensed tanins are classified according to their molecular structure (RIBEREAU-GAYON, 1968).

1.1.6. Traditional and common use of *Asparagus sp*

In traditional Chinese medicine, roots were commonly employed for the treatment of non-specific inflammatory conditions, the prevention of kidney and bladder stones, hydropysis, rheumatism, liver disease, bronchial asthma, gout, irritable cough, dry mouth, throat, and constipation. Furthermore, the grass, rhizome, and root were employed in the medical field.

According to Shao Y, et *al*., (1996), It has been demonstrated that certain activities have antitumor and antifungal immunostimulants and diuretics effects **(Balansard and Rayband, 1987)**. Aantioxidant properties of asparagus have also been proven **(Rodriguez, et *al*., (2005).** According to **Ali and Khan (2009),** traditional healers claim that the seeds of A. officinalis possess anti-diabetic properties.

- **Antimicrobial effects**

An antimicrobial agent is defined as any chemical, physical or biological agent that prevents the growth and/or survival of microorganisms. These substances have an affinity for cells of parasites and capacity to kill them more effectively than the damage they cause to the body. This allows for the destruction of the parasites without significant disruption to organism.

- **Anti-cancer, antioxidant and hypolipidemic effects**

It has been demonstrated that *Asparagus officinalis* may prevent occurrence of genetic mutations that precede the development of early-stage cancers **(Abdulmajed et *al*., 2005).** stimulates the production of phase II detoxification enzymes, thereby eliminating cancer-causing drugs and supporting liver function. **Hamet (2003)** notes its synergy between the two substances in enhancing antioxidant activity. It has been demonstrated that this compound may inhibit tumour formation by suppressing chronic inflammation **(Ahmad et *al*., 2012).** Furthermore, it has been demonstrated that this product can improve digestive and immune health **(Albano, 2010).**

Aasparagus saponins demonstrated a dose-dependent increase in reactive oxygen and Ca2+ species, a reduction in pH, activation of the mitochondrial permeability transition pore, and a reduction in membrane potential over a 24-hour period.

Furthermore, treatment resulted in an increase in caspase 9 and caspase 3 activity, a decrease in Bcl2 expression, an increase in Bax expression, and release of CytC and subsequent activation of caspase 3 **(Ji et *al.*, 2010).**

Studies demonstrated that an extract derived from asparagus by-products exhibited hypolipidemic effects in mice fed a high-fat diet. Following eight weeks of treatment at 40, 80, and 160 mg/kg, total cholesterol and low-density lipoprotein levels were reduced, while high-density lipoprotein and various serum enzymes were increased. Additionally, weight gain was observed **(Zhu et *al.*, 2011; Zhou et *al.*, 2010).**

1.2. Extraction of active ingredients from plants

I.2.1. Different treatment of plants

- **Solid-liquid extraction**

Process of solid-liquid extraction involves the transfer of material from a plant to a liquid solvent, such as chloroform, methanol, or water, for the purpose of extraction (Herodez, 2003; Clémentine, 2012).

The extraction process comprises a number of distinct stages, including solvent solvation, surface desorption, and the transport of the compound into the extraction liquid (Dean, 1996).

- **Liquid-liquid extraction**

Once plant material has been contacted by an organic solvent, water is added and extraction is carried out with a water-immiscible solvent. Sample is extracted, the solvent is evaporated, and the residue is reconstituted for analysis. Use of solvents of varying polarities allows for the separation of active molecules. According to Bouzid (2011), this involves metabolites diffusing between two non-miscible liquid phases.

1.2.2. Current extraction techniques

1.2.3. Ultra Sonic extraction

Ultrasonic-microwave cooperative synthetic method was subjected to investigation. Combination of intense dispersion and stirring effects of ultrasound with homogeneous heating by microwave radiation was exploited to achieve the desired outcome (Zhe Jiao, et *al.*,2016)

1.2.4. Extraction by rotavapor

Evaporation of solvent is a crucial step in the analytical procedure, as it affects the recovery of the analyte (Łukasz Dąbrowski, 2016). Instrument has a wide range of applications in diverse fields, including organic chemistry, pharmaceutical research, and food analysis. Utilisation of gentle heat, vacuum, and rotation enables the precise separation of solvents from samples, thus facilitating the isolation of desired compounds. This process is known as a rotary evaporator, or rotavap

1.3. Notions of Pharmaceutical forms

Selection of the galenic form is contingent upon the route of administration. Despite the ongoing expansion of possibilities resulting from the success of Galenic research in this area, a limited number of common forms are almost always used. In the majority of cases, one or two alternatives are available. With regard to the oral route, the most frequently adopted form is that of the tablet, with the capsule form being employed somewhat less frequently. These solid unit doses offer several advantages, including well-preserved stability, suitability for outpatient treatments, and the ability to be manufactured with precision and high yields on an industrial scale (Alain et *al*., 2009).

1.3.1. Solid oral forms

1.3.1.1. Tablets

Forms of variable appearance are often rounded, solid and compact, and consist of one or more active ingredients and excipients (Talbert et *al*., 2009).

Tablets are manufactured by compressing particles and are intended for oral or vaginal administration. Tablets can be swallowed, crushed, dissolved in water, or kept in mouth to release the active substance (International Pharmacopoeia, 1980; kouonang, 2005).

1.3.1.2. Uncoated tablets

Uncoated tablets may be classified as single-layer tablets or multi-layered tablets, which are arranged in parallel or in a concentrated configuration (Alain et *al*., 2009; European Pharmacopoeia, 2014).

1.3.1.3. Coated tablets

Tablets of this category are composed of a surface coating of a mixture of substances, including resins, polymers, rubber, sugars, plasticizers, polyols, waxes, and dyes. When the coating is of a very thin consistency, it is designated as a film coating (Alain et *al*., 2009; European Pharmacopoeia, 2014).

1.3.1.4. Special tablets

A number of different categories of special tablets exist, with most significant of these being effervescent, soluble and dispersible tablets.

1.3.1.5. Effervescent tablets

Effervescent tablets are uncoated and release carbon dioxide in water. Prior to use, tablets must be dissolved in water (European Pharmacopeia, 2011)

1.3.1.6. Soluble tablets and dispersible tablets

Soluble or dispersible tablets, whether uncoated or film-coated, are soluble or dispersible in water prior to use, resulting in a slightly opalescent solution (European Pharmacopoeia, 2011). Orodispersible tablets are designed to be rapidly dispersed in oral cavity prior to swallowing (European Pharmacopoeia, 2011).

1.3.1.7. Capsules

Capsules are solid pharmaceutical preparations encased in hard or soft (gelatin-based) shells, containing a single dose of medication. They can accommodate solid, liquid, or paste contents. Hard capsules are manufactured with rigid shells, while soft-coated capsules are formed, filled, and sealed in a single manufacturing cycle (European Pharmacopoeia, 2011; Vidal, 2011). According to Alain et *al*., (2009), The capsule categories include hard envelope, soft envelope, gastro-resistant, modified release, and stamped capsules.

1.3.1.8. Powder

Aforementioned preparations comprise solid, dry particles that have been mixed with active ingredients and pre-dried excipients. Furthermore, they can be effervescent (Champe et *al*., 2000 ; Talbert et *al*., 2009).

1.3.1.9. Granules

Granulates are dry solid grains that form aggregates of powder particles. Granulates exhibit considerable variation in size, shape, and porosity. Subsequent to dissolution or suspension in water, they may require crushing or absorption (Alain et *al.*, 2009; Talbert et *al.*, 2009).

1.3.2. Liquid oral forms

Liquid oral preparations, which may take the form of solutions, emulsions, or suspensions, contain active substances that have been dissolved in a suitable vehicle. Advantages include pre-dissolution of active ingredients and fractioning for multi-unit forms. However, potential disadvantages include the possibility of alteration by gastrointestinal secretions and variable absorption and bioavailability (Pebret, 2005).

1.4. Methods of manufacture of tablets

Tablets, which are oral pharmaceutical forms, are manufactured by compressing a formulation of active ingredients and excipients in order to enhance the product's properties (Lieberman et Lachman, 1980; Osol et *al.*, 1980). specific physical characteristics of ingredients, such as good flow, cohesion, and lubrication, are essential for the successful preparation of a given recipe (Moufarej, 2012). Manufacturing methods employed to achieve these characteristics include wet granulation, dry granulation, and direct compression (Lieberman et Lachman, 1980; Osol et *al.*, 1980). Each method has its own set of advantages, disadvantages, and specific applications. Direct compression is the simplest method, while wet granulation is the most common (Lieberman et Lachman, 1980).

1.4.1. Wet granulation

Wet granulation method is considered the oldest and most common for tablet production (Lieberman et Lachman, 1980), process involves the conversion of small, irregular particles into larger, homogeneous granules through the application of moisture and heat (Armstrong, 2007; Miyachi et *al.*, 2009; Gopinath, 2013). This process enhances the flow and compressibility of the material, thereby facilitating the compression of tablets (Levacher, 2006; Guigon et Saleh, 2009). Other advantages include uniform distribution of ingredients, enhanced flow properties, prevention of segregation, and production of stronger tablets (Alderborn et Nystrom, 1996; Augsburger et Zellhofer, 2007; Singh et Naini, 2007). However, the process is costly due to the necessity of multiple stages, the use of time, equipment, energy, and space (Lieberman et Lachman, 1980; Osol et *al.*, 1980).

1.4.2. Dry granulation

In contrast to wet granulation, dry granulation does not utilise heat or moisture (Vaubourdolle, 2007). It is employed when direct compression is not feasible due to suboptimal formulation characteristics or when wet granulation cannot be utilized due to heat- or moisture-sensitive ingredients (Lieberman et Lachman, 1980). Formation and subsequent disintegration of lingots during the aforementioned process results in the creation of uniform granules that are suitable for compression. Although this process reduces equipment, space, production costs, and time, it also entails a significant amount of material to be recycled and the potential for component segregation (Lieberman et Lachman, 1980).

1.4.3. Direct compression

Direct compression is a process whereby tablets are formed without the use of pre-grain processing (Osol et *al.*, 1980; Ribet, 2003). Formulation has been in use since the 1950s and relies on the use of special excipients, including vaporized lactose, micro-crystalline cellulose, and starch (Lieberman et Lachman, 1980). This method offers economic benefits by reducing the number of required process steps, the number of necessary equipment items, and the energy consumption associated with the process (Lieberman and Lachman, 1980; Osol et *al.*, 1980; Torrelló et *al.*, 2003). Elimination of issues related to heating and humidity enhances product stability (Ribet, 2003) . Furthermore, the material is optimal for the rapid dissolution of pharmaceuticals due to the enhanced disintegration of tablets (Lieberman et Lachman, 1980).

1.4.4. Stability of medicines

Stability of a medicinal product can be defined as its capacity to maintain its chemical, physical, microbiological and biopharmaceutical properties within specified limits throughout its validity period. Stability of pharmaceutical preparations is contingent upon both intrinsic and extrinsic parameters, including temperature, humidity and light. Such factors include those related to the raw materials, pharmaceutical form and packaging (Singh, 1999; Health Canada, 2003).

Asparagus officinalis, or asparagus, is a medicinal plant known for its diuretic, anti-inflammatory, antioxidant and immunomodulatory properties, thanks to its bioactive components such as saponins, flavonoids and phenolic acids. This study aims to develop two galenic forms of this plant: a syrup and tablets. The syrup is chosen for its ease of administration, especially suitable for children and the elderly, while the tablets offer increased convenience and stability.

The study aims to create effective and stable formulations, preserving the pharmacological properties of *Asparagus officinalis*. The methodology includes the extraction of active ingredients, the formulation of products, and the evaluation of their stability and efficacy. The following section will describe in detail the materials and methods used in this process.

2. Preparation of the powder

2.1. Plant Collection and preparation of the plant

Region of the harvest is Berghouth Chreaa Blida, in the late winter Period. plant is drying in an empty room at moderated temperature. Then, plant is grinding in an electric shredder.

2.2. Extraction of the active substance by maceration and rotavapor system

Extraction of the active substance is divided into two parts, firstly maceration and rotative evaporation in order to eliminate le solvent.

2.2.1. Maceration step

Extraction of the active substance was carried out using the maceration process. This process consists of mixing 10 g of the plant in 150 ml of a 50% ethanol 50% disstilated water solvent mixture and putting it in an ultrasonic bath for 45 minutes at a temperature of 40°C. then we filter with the help of a pump.

Ethanol is added to the resulting mixture. The latter is rotated to increase the evaporation surface and then the pressure is reduced, usually thanks to a water pump.

Figure 2: Ethanolic extract stirring and filtration step

2.2.2. Vacuum Rotary evaporator step

Rotary evaporator is based on (partial) vacuum distillation. rotational speed and vacuum created allow evaporation at temperatures lower than the evaporation temperatures of the solutions to be evaporated.

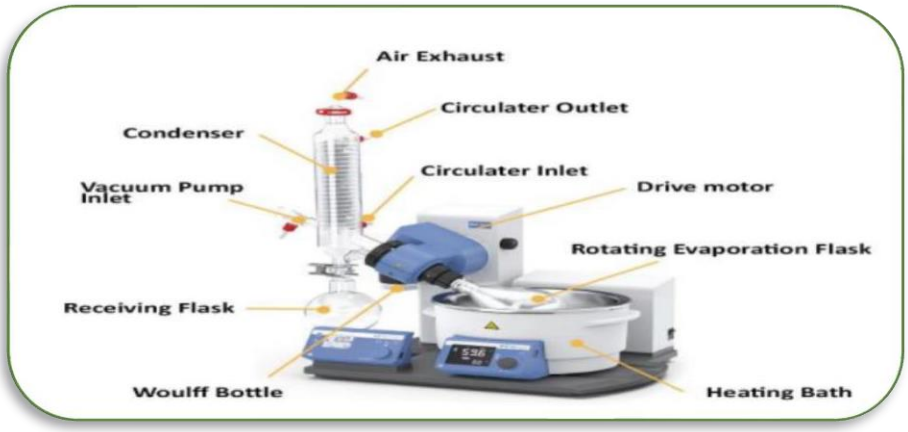


Figure 3 : Vacuum rotavapor

Rotavapor based on vacuum distillation, begins by placing the macerate to be evaporated in the evaporation flask. Then, the tank is rotated and the cold-water tap connected to the refrigerant is opened.

After that, the valve connecting the assembly to the external pressure is closed and the vacuum inside the apparatus is made using a water horn. If the evaporation is not fast enough, the evaporation flask is immersed in a water bath of hot water.

Evaporation continues until the solvent disappears completely. Finally, the shut-off valve is opened to restore the atmospheric pressure inside the device, and then the water in the refrigerant and water tube is turned off.

2.3. Extract characterization

2.3.1. Phytochimique Screening

The methanolic extracts were subjected to various phytochemical tests in order to establish the major chemical groups contained in these methanolic extracts, using the standard method based on staining and precipitation reactions.

- **Polyphenols:** Two millilitres of extract are treated with 1ml of 1% FeCl3, the appearance of a staining blackish-blue or more or less dark green is a sign of the presence of phenols.
- **Flavonoids:** To 1 ml of each extract a few drops of concentrated hydrochloric acid (HCl) are added and a few milligrams of magnesium (Mg). The presence of flavonoids is confirmed by the appearance of the color red or orange.

- **Tannins:** To detect the presence of tannins, a few drops of FeCl3 at 1%. The colour changes to blue black in the presence of gall tannins and to greenish-blue in the presence of presence of catechetical tannins (condensed tannins).
- **Saponins:** To 5ml of each extract is added 10ml of distilled water, the whole is stirred energetically in the horizontal position for 15 seconds. Then, the mixture is left to rest for 15 minutes. Persistence of the foam of at least 1 cm for 15 min indicates the presence of saponins.
- **Free quinones:** On one volume of each extract a few drops of 1% NaOH are added. The Apparition of a colour that turns yellow, red or purple indicates the presence of free quinones.
- **Terpenoids:** To 5 ml of each extract is added 2 ml of chloroform and 3 ml of concentrated sulphuric acid, the formation of two phases and a brown colour at the interphase indicates the presence of
- terpenoids.

2.4. Syrup Formulation

Syrup we preparate with MODD 6 using active substances and excipients which are given in the table below

2.4.1. Excipients in the syrup formulation

Different excipients used in the formulation of the syrup are given in the table below.

Table II. Excipients commonly used with a base and an active ingredient in a syrup and their role

Excipients	Role
Purified water	Main solvent of syrup
Propylene glycol	Solvent and humectant that helps preserve the aroma and texture of the syrup.
Hydroxy propylcellulose	A synthetic viscosizing agent that gives syrup a thick, transparent texture.

In order to build the experiment matrix, we chose to use the software MODDE 6.0 statistics. By introducing the different factors and their range of variation, namely: plant powder

[15%], Saccharose [30-35%], propylene glycol [25-30%], HPMC (hydroxypropyl methylcellulose) [10-20%], and the table below show the matrix.

Given the objective of this study, the responses are Rheology and organoleptic proprieties. Obtained matrix of the different formulation given by the MODDE 6 are shown in the table below.

Table III. Table of Syrup Formulation Matrix Table (MODDE 6.0)

Exp No	**propylene glycol**	**HPMC**	**saccharose**
1	0	0,5	0,5
2	1	0	0
3	0	0	1
4	0,5	0,5	0
5	0	0,333	0,667
6	0	0,167	0,833
7	0,667	0	0,333
8	0,333	0	0,667
9	0,833	0,167	0
10	0,667	0,333	0
11	0,375	0,25	0,375
12	0,375	0,25	0,375
13	0,375	0,25	0,375
14	0,375	0,25	0,375

2.4.2. Preparation of syrup according to the European Pharmacopoeia:

preparation of the syrup consists to start by weighing the sucrose and placing it in a beaker. Add about 50g of purified water, then heat the mixture on a hot plate to about 80°C, stirring constantly until the sucrose is completely dissolved. Top up the volume with purified water

until you get 100 g, then mix and filter the syrup hot through a paper filter. Allow the syrup to cool to room temperature before adding 20 g of liquid extract. Then weigh the propylene glycol according to the matrix, place it in the beaker, and stir until completely dissolved. Finally, weigh the hydroxypropyl cellulose, add it to the beaker, and stir well.

2.4.3. Characterization of syrup

characterization of syrup consists of two analyses: rheology tests, organoleptic and pH test.

2.4.3.1. Rheology tests

Rheological characterization of the suspensions aims to study the influence of variation in the concentrations of formulation parameters on their behaviour rheological. Because the resistance to flow of suspensions is linked to the rigidity of the network of particles formed within the liquid; rheology therefore allows a measurement macroscopic force required to overcome flow resistance, as well as to evaluate the stability and ease of setting at the time of use. So, all the elements obtained during this study make it possible to identify the domain of variation, at which the suspensions exhibit interesting rheological behavior.

This characterization includes the study of the rheological behavior of the suspensions prepared. The measurements were carried out using a plane-plane system with a ramp increasing in shear speed from 0.000995 s-1 to 1000 s-1, the measurement time between two successive points is 5s. Viscosity curves are given in terms of apparent viscosity as a function of the shear speed (gamma point).

2.4.3.2. pH Test

pH is measured in the formulated syrup to ensure its quality, stability, and efficacy. Variations in pH can indicate formulation or contamination issues, while specific pH levels can promote the stability of active ingredients. In addition, some drugs may have better absorption or biological activity at specific pHs. Finally, pH measurement is often a regulatory requirement for pharmaceutical products, ensuring compliance with current standards.

2.5. Preparation of the plant-based tablets:

Formulation concerns "all the operations carried out during the mixing, combining or shaping of ingredients (one or more active ingredients and excipients) in order to obtain a commercial product characterized by its function of use and its ability to meet per-established

specifications". Understanding the phenomena involved in formulation facilitates the optimization of preparation.

There are different dosage forms generally classified according to route of administration or physical condition. Each shape has advantages and disadvantages. It was chosen to focus on tablets, the most common solid pharmaceutical form.

For the formulation of the tablets, design of experiments (MODDE 6.0) was used as a planning method in order to:

- Minimize the number of attempts;
- Specify the experimental error;
- Controlling for error due to the environment, external factors independent of the user by means of analysis of variance.

2.5.1. Construction of the experiment matrix:

In order to build the experiment matrix, we chose to use the software MODDE 6.0 statistics. By introducing the different factors and their range of variation, namely: plant powder [15%], sucrose [30-35%], lactose [25-30%], potato starch [10-20%], magnesium stearate [5-10%]. And the table below show the matrix

Given the objective of this study, the responses are:

Friability (%), flow (s), Carr Index IC (%), settlement. The most appropriate experimental planning strategy is the surface study of responses. The matrix of experiments responding to this strategy is of the D-Optimal type.

Table IV. Table of Matrix of experiments in centered and reduced variables

N°	**Asparagus**	**Saccharose**	**Lactose**	**Stretch of potato**	**Mg stearate**
1	0,15	0,33	0,26	0,2	0,05
3	0,15	0,31	0,28	0,2	0,05
4	0,15	0,30	0,30	0,16	0,08
7	0,15	0,35	0,25	0,15	0,10

8	0,15	0,30	0,28	0,16	0,10
9	0,15	0,35	0,3	0,1	0,1
10	0,15	0,35	0,30	0,15	0,05
11	0,15	0,35	0,275	0,15	0,075
12	0,15	0,32	0,27	0,16	0,078
13	0,15	0,30	0,25	0,2	0,10

2.5.2. Tablet formulation steps:

2.5.2.1. Characterization of the active ingredient and excipients used:

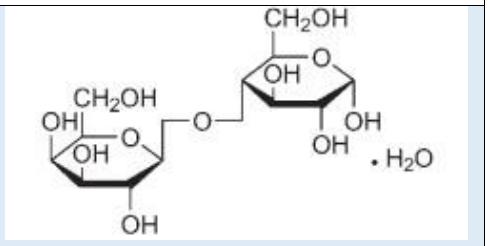
Active ingredient:

Asparagus officinalis

Excipients:

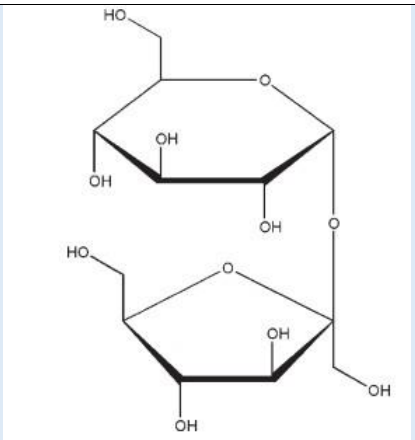
Excipients are substances of chemical or natural origin that facilitate the use of the drug but do not have a curative or preventive effect. They are inactive with regard to the pathology. We have chosen its excipients in order to facilitate the administration and preservation of the active ingredient.

Table V tablets Formulation Excipients and their role

Lactose monohydrate	
Lactose monohydrate or lactose alpha-monohydrate is a natural disaccharide, obtained from milk, which consists of a galactose and a glucose fragment.	
Saccharose	

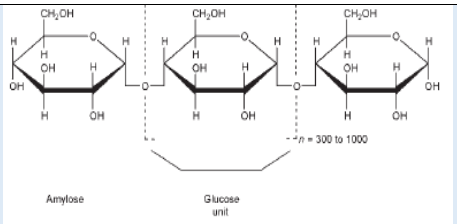
Saccharose is a sugar obtained from sugar cane, sugar beet, and other sources. It does not contain any added substances.

Saccharose occurs in the form of colourless crystals, crystalline masses or blocks, or white crystalline powder; It is odorless and has a sweet taste. Its crude formula is $C_{12}H_{22}O_{11}$ and its molecular weight is 342.30 g/mol.



Potato stretch

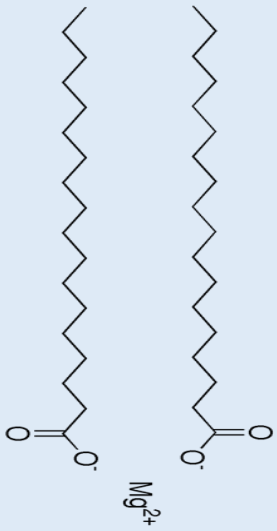
Potato stretch is mainly composed of two types of carbohydrate molecules: amylose and amylopectin



Magnesium stearate

Magnesium stearate is the magnesium salt of stearic acid, which is chemically better known than octa-decanoic acid.

Magnesium stearate is a very fine impalpable powder, light white in color, precipitated or ground, with an alkaline pH, solid at room temperature, it melts at about 88°C and it is not soluble in water, of low bulk density, having a slight stearic acid odour and a characteristic taste. The powder is greasy to the touch and adheres easily to the skin. Its crude formula is C_36 H_70 MgO_4 and its molecular weight is 591.24 g/mol.



2.5.2.2. Tablet manufacturing

protocol Preparation of the powder

mixture

Respective quantities of the different components of the mixture are weighed separately: the active ingredient asparagus, a diluent and bulking agent (sucrose, lactose), a binder (potato starch), and magnesium stearate as a compression lubricant.

In a container, 15 grams of the plant's powder are put in the respective quantities

previously sieved excipients and then mixed in a mixer/granulator for 15 minutes.

2.5.2.2.1. Compression:

Preparation of tablets by compression using an instrumented FROGERAIS alternative tablet. Protocol is as follows:

2.5.2.2..2. Feeding: Upper punch is raised. Lower punch is in the down position. The hoof is located above the compression chamber, which is filled with grains by simply flowing the powder.

2.5.2.2.3. Levelling: Punches are in the same position. Wedge moves horizontally by leveling the powder at the top level of the die.

2.5.2.2.4. Compression: Lower punch does not move. Upper punch descends abruptly and compresses the grain with force.

2.5.2.2.5. Ejection: Upper punch lifts up; it returns to its original position. Bottom punch rises and brings the tablet to the upper level of the die. Wedge returns to its starting position by moving the tablet to an evacuation chute, and simultaneously fills the compression chamber for the next operation.

2.6. Pharmaco-technical controls during manufacturing:

There are various pharmaco-technical controls to be carried out during manufacturing, namely:

2.6.1. Flow velocity measuring

Flow test is intended to determine, under defined conditions, the ability of divided solids (powder, granules, etc.) to flow vertically. Test is carried out according to the latest edition of

the European Pharmacopoeia (EP.6, 2010). A time of less than or equal to 10 seconds is considered to be good flow.

After pouring a mass of 1 grams of powder into a standardized funnel. We repeated the operation 3 times and we noted the time, then we calculated the average.

Figure 4. Flow velocity measuring device

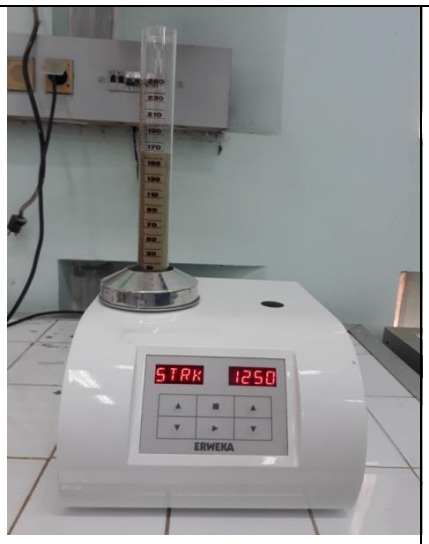


Figure 5. Compacting powders device.

Figure 6. Sieving device

2.6.2. Settlement:

Purpose of the apparent volume test is to determine, under defined conditions, 150-gram apparent volumes of the powder mixture before and after settlement, and then to determine the suitability for settlement, as well as the bulk density of divided solids (e.g. powders, granules). Test is carried out according to the European Pharmacopoeia 6th edition.

In a 500 ml dry test tube graduated to 2 ml, we introduced1 g of powder without compacting, and we read the apparent volume, then weV_0 subjected the test tube to 10 and 50 and 500 blows, and we noted the apparent volumes.

Table VI. Evaluating flowability using Carr's Index and Hausner Ratio.

Carr's Index (%) (Compressibility Index)	Flowability	Hausner Ratio
01-11	Excellent	1.00 – 1.11
11-15	Good	1.12 – 1.18
16 - 20	Fair	1.19 – 1.25
21 - 25	Passable	1.26 – 1.34
26 - 31	Poor	1.35 – 1.45
32 - 37	Very Poor	1.46 – 1.59
> 38	Extremely Poor	> 1.60

Carr's Index (IC):

$$IC = \frac{Vbulk - Vtapped}{Vbulk} \times 100$$

Hausner Ratio (IH):

$$IH = \frac{Vtapped}{Vbulk}$$

Vbulk is the bulk volume

Vtapped is the tapped volume.

2.6.3. Particle size analysis:

We passed a quantity of 150 grams of powders through a series of mesh opening sieves ranging from 100 to 800 µm. Then we turned the device on for 30 minutes.

2.7. Pharmaco-technical controls at the end of production:

These controls are tests that must be carried out to ensure that our product meets the standards of the European Pharmacopoeia.

2.7.1. Friability:

According to the monograph of the European Pharmacopoeia, friability test is carried out on a sample of ten tablets weighed before and after the test. Mass loss should be less than 1%.

With using ELECTROLAB friabilator we use our tablets with a unit mass of 1200 mg, we took 10 tablets. Then we placed them on a sieve and removed the free dust with a soft brush. We weighed them precisely and placed them in the drum. We did 100 rotations and then we took

the tablets out of the drum. Then we removed the free dust, and then weighed it exactly. Friability is calculated by the following equation:

$$F\% = \frac{\text{masse d'échantillion avant essai} - \text{masse d'échantillion aprés essai}}{\text{masse d'échantillion avant essai}} \times 100$$

Figure 7 Friability measuring device.

Figure 8. Hardness measuring device.

2.7.2. Hardness:

Hardness testing, which is significant in quality control and formulation development procedures. This analysis evaluates the force required to crush a tablet" by applying a diametrical force to it.

Trial is carried out on 10 tablets according to the monograph of the European Pharmacopoeia.

We took a sample of 10 tablets and placed them between two jaws, tablet is oriented horizontally in the device. We measured the maximum force required for the tablet to break, expressed in NEWTON (N) using ELECTROLAB durometer.

2.7.3. Dissolution:

in vitro dissolution test applied to the tablets is intended to determine their greater or lesser ability to pass into solution in a given medium of PA. The passage into solution is assessed by

determination of the PA in samples taken from the dissolution medium at different time intervals. The in vitro dissolution test of uncoated tablets is the main test performed to monitor the "in vitro availability" of the PA they contain.

1.paddle box 2. dissolution cup 3. water bath 4. the keypad 5. screen

Figure 9. Dissolutest device.

Disolutest apparatus used for this test is composed of eight cylindrical containers. And a hemispherical bottom with a capacity of 1L, which can be covered, in inert transparent material. This later is partially immersed in a thermostatic water bath to maintain a temperature of 37 ± 0.5°C inside the container during the test and to ensure a smooth and constant movement of the dissolution medium. A motor and agitator consisting of a blade and a rod, its rotation is uniform and without significant oscillation likely to affect the results. The blade and stem are made of rigid and inert material.

operating conditions of the dissolution test are:

- Device: ERWEKA (paddle)
- Dissolution medium: HCl, KH_2PO_4
- pH: 1.2 and 5.8 and 4
- Stirring speed: 100 tr/min
- Middle temperature: 37 °C
- Dissolution Volume: 900 ml

We placed the tablets in the eight vases of the device in a medium simulated to the gastric environment with a given volume (900 ml), we set the temperature to 37°C. Then we took 5 ml manual samples of the dissolution medium from each vase every 5, 10, 15, 20, 25, 30, 35,

40, 45, 60, and 90 minutes. We passed the samples through a UV spectrophotometer by fixing the wavelength at 268 nanometers to obtain the absorbance that is translated into the dissolved % of active ingredient from the plot of the calibration curve that we obtained by diluting different quantities of the active ingredient in the medium.

And we calculate le rendement par minutes $rendement = {}^{ABSn}/_{ABSc}$ **Eq II.4.**

ABSn absorbance of each formulation lot

ABSc Initial absorbance (The initial absorbance of the active sustance in the tablet)

and the tables below represent the results

In this part of our work, we will present all the results and their discussions

3.1. Results of characterization of the extract substances

3.1.1. Phytoscreening:

Qualitative assay results of the secondary metabolites

Table VII table represents presence of secondary metabolites in the ethanolic extract

Secondary metabolites	Presence
polyphenols	High Presence
flavonoids	High Presence
Tannins	Low Presence
Saponins	High Presence
Free Quiñones	Low Presence
terpanoides	High Presence

This table represents results obtained by colouring that appeared in the end of the test we notice that there is a high presence of polyphenols and a presence of flavonoids and saponins and terpanoids and a low presence of quinones and tannins.

3.2. Results of Syrup characterizations tests :

3.2.1. Organoleptic proprieties

Visual inspection of the final prepared suspension. After mixing all the excipients, the final suspension should be well homogeneous cream colour.

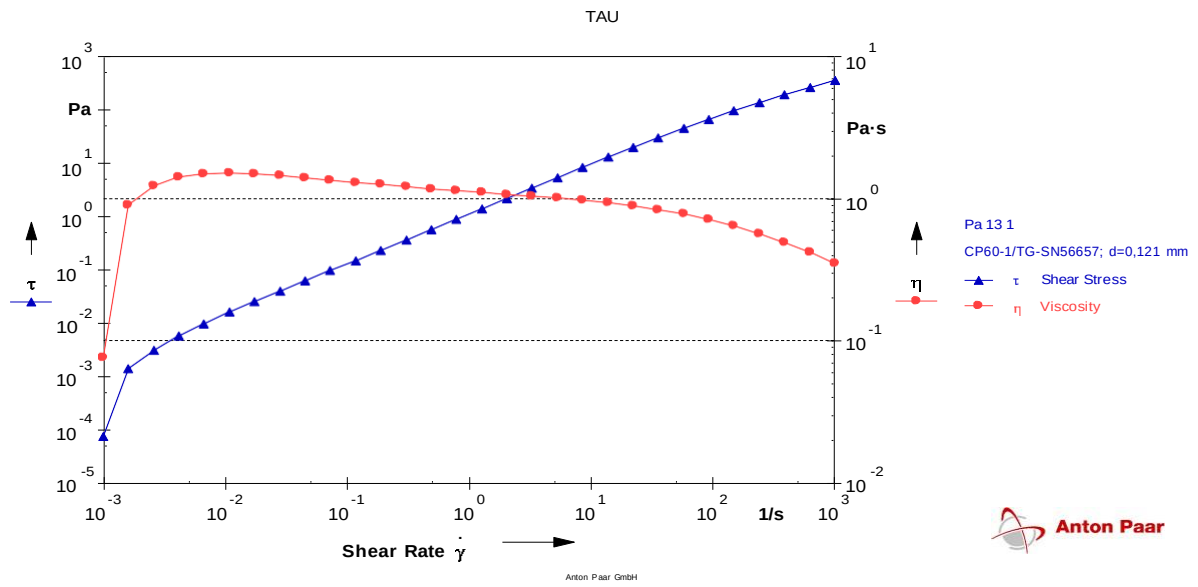
Figure 10 Visual appearance of the syrup

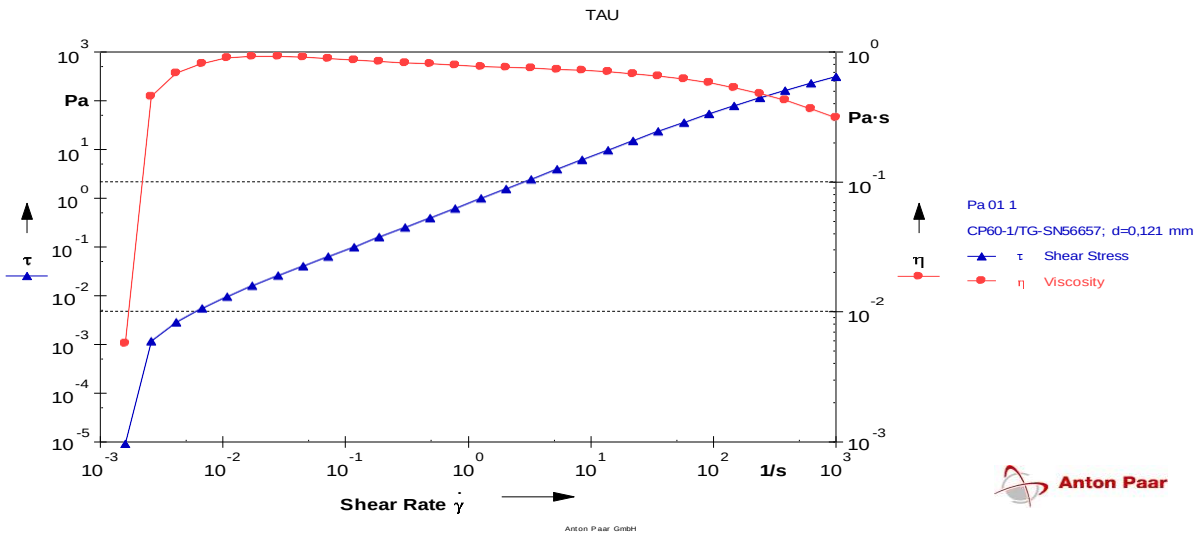
3.2.2. Rheology Test

Characteristics of the suspensions vary with different factors, notably with the nature and portion of the excipients. Furthermore, during their conservation it is necessary be able to guarantee good homogeneity or easy resuspension by simply manual agitation.

Obtained results of rheology of the different syrup formulation are given in the figure below, all the numerical results are shown in the annex.

1





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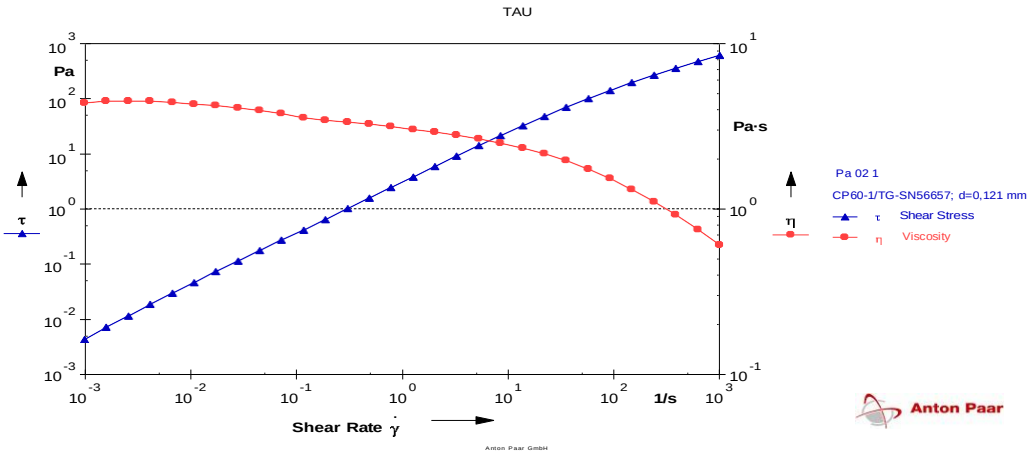
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Anton Paar
Anton Paar GmbH

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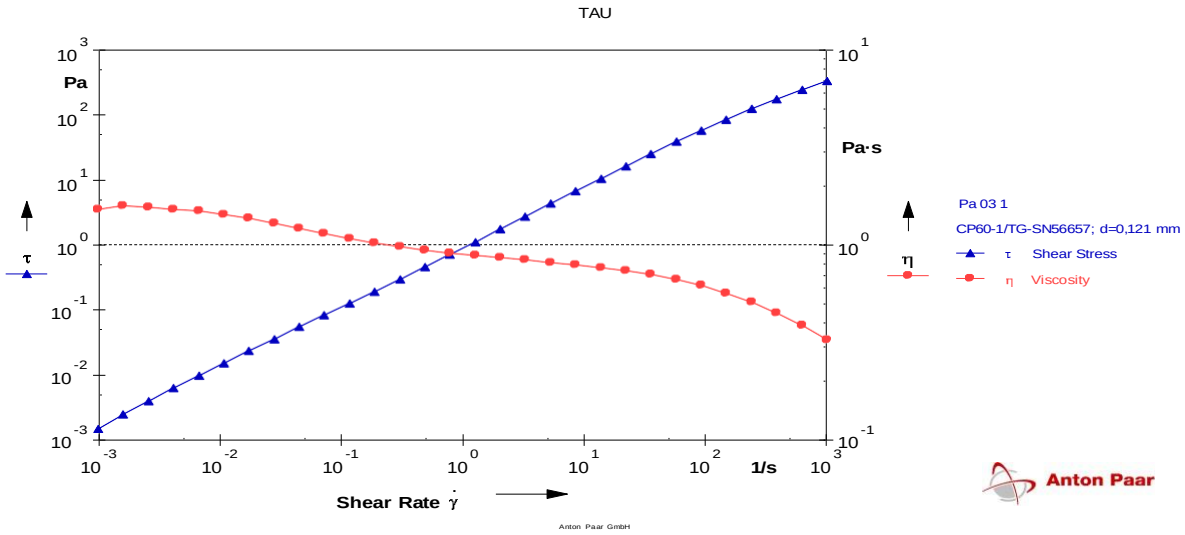
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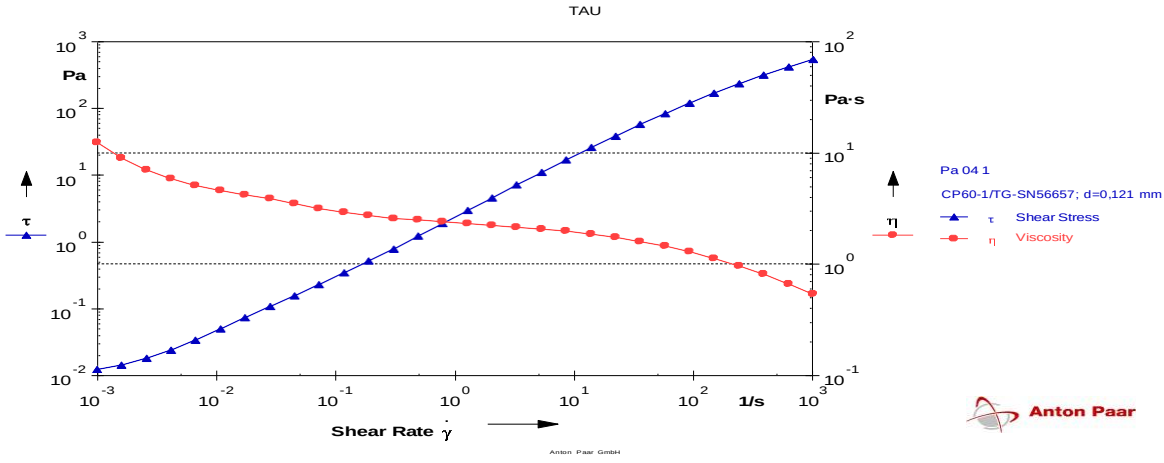
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Anton Paar GmbH

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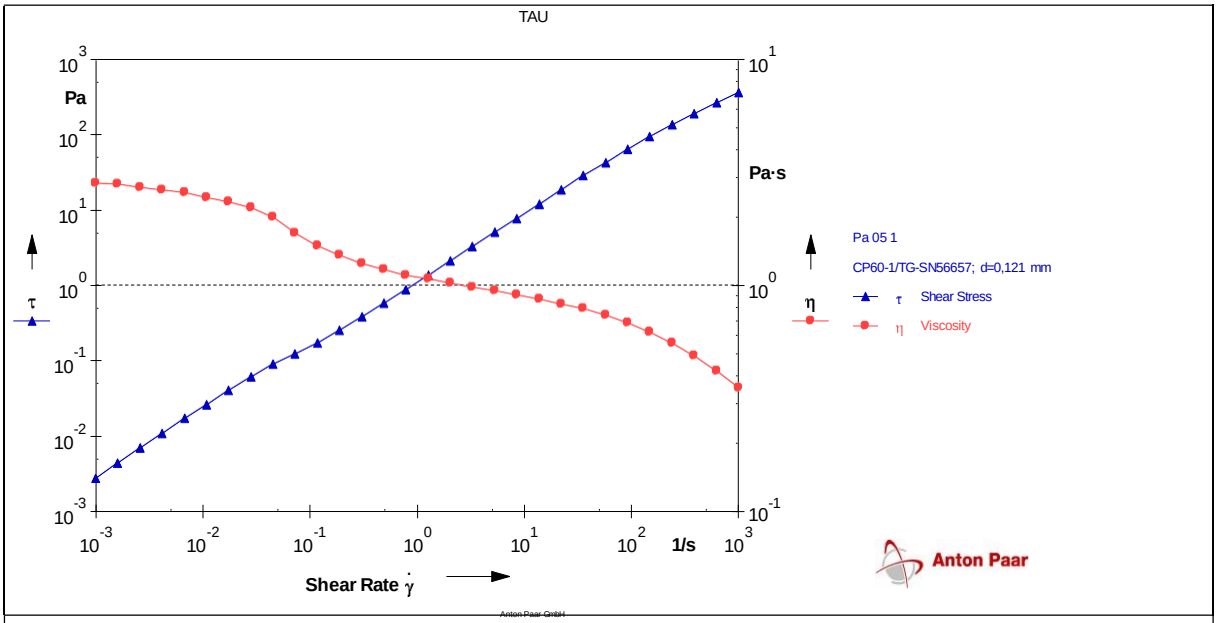
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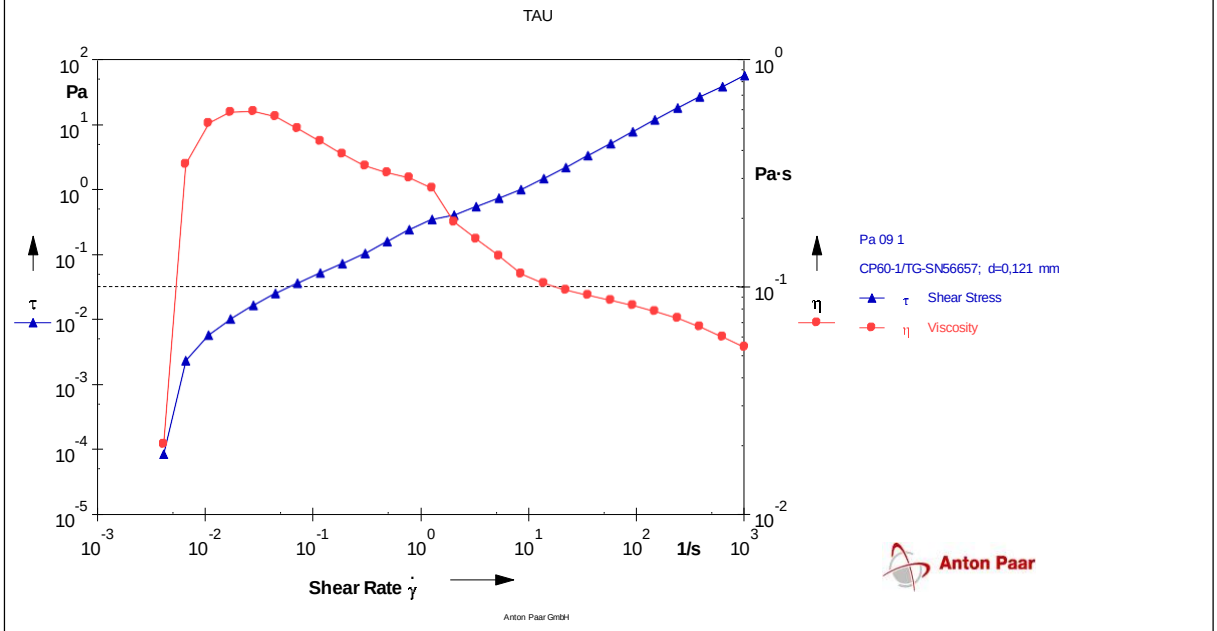
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Anton Paar
Anton Paar GmbH

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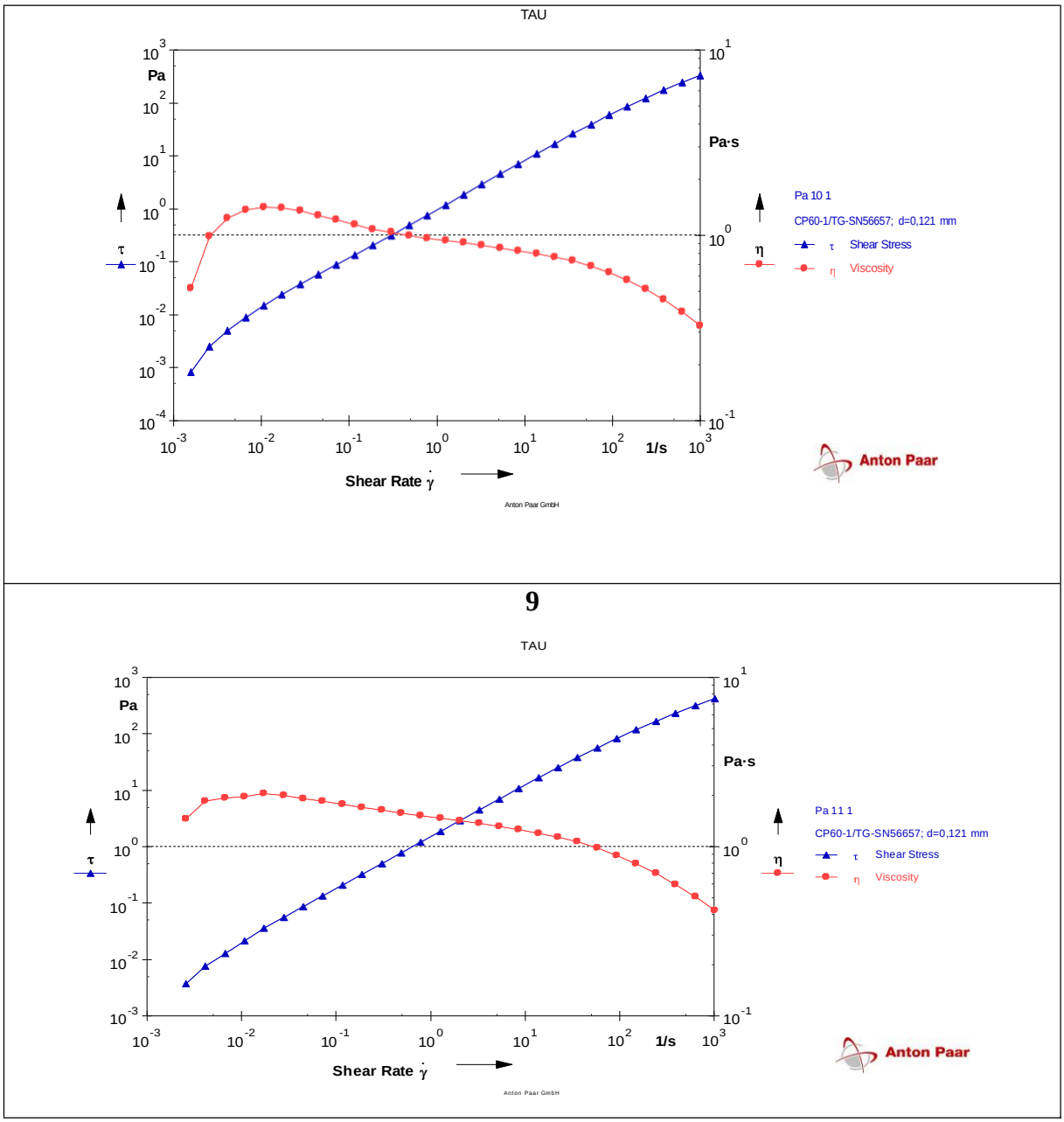


Figure 11 Rheologie test results

In this part, we present the study of the rheological properties of the different suspensions (the 10 batches of syrup). Two parts of the evolution of viscosity can be observed: a first domain characteristic of a Newtonian behaviour (constant viscosity as a function of shear velocity) and a second typical of a rheo-fluidifying system (the decrease of viscosity as a function of shear velocity).

3.2.3. pH TEST

With a pH meter we measure the pH in our syrup samples and the results are presented in the following table

Table VIII Results of pH measurments

The Formulations	pH
Formulation 1	6.14
Formulation 2	5.78
Formulation 4	6.13
Formulation 5	5.83
Formulation 9	5.34
Formulation 10	6.03
Formulation 11	6.13
Formulation 13	5.63
PLAS	5.32
Formulation 3	5.9

This table represents the pH measurement results of each batch of syrup and it can be seen that the pH of syrup for all formulation is conformed to use.

3.3. Results of technology proprieties

3.3.1. Settlement and flow:

Tests are carried out on the compression granules in order to guarantee the quality of the tablets. Settlement tests (Carr Index) evaluate the compressibility of the granules, while flow tests (Hausner Index) measure their fluidity. These analyses make it possible to optimize the formulation, design suitable equipment, and ensure rigorous quality control. All the results are given in the tables below.

3.3.1.1. Flow :

Flow test is done to find out the flow time of the granules and the obtained results are illustrated in the following table:

Table IX Flow test results of different formulations

Lots	Time (seconds)
Formulation 1	8.94
Formulation 2	7.29
Formulation 3	7.55
Formulation 4	7.6
Formulation 7	7.18
Formulation 8	8.29
Formulation 9	8.22
Formulation 10	7.54
Formulation 11	7.6
Formulation 13	7.01

Flow of grains from the different tests is good given that they all flow in less than 10 seconds. We notice that the results are compliant according to the European Pharmacopoeia 2010 all the results do not exceed 10s

3.3.2.1. Settlement:

A compaction device measures the following results shown in the table below

TABLE X Settlement test results

Formulations	Volume (ml)	IC
Formulation 1	V0 = 270 ml	6
	V10 = 250 ml	
	V50 = 240 ml	
	V500 = 235 ml	
Formulation 2	V0 = 280 ml	5.66
	V10 = 265 ml	
	V50 = 255 ml	
	V500 = 250 ml	
Formulation 3	V0 = 275 ml	7.54
	V10 = 265 ml	
	V50 = 255 ml	
	V500 = 245 ml	
Formulation 4	V0 = 265 ml	7.84
	V10 = 255 ml	
	V50 = 248 ml	
	V500 = 235 ml	
Formulation 7	V0 = 265 ml	4.76
	V10 = 252 ml	
	V50 = 242 ml	
	V500 = 240 ml	
Formulation 8	V0 = 270 ml	5.09
	V10 = 255 ml	

	V50 = 245 ml	
	V500 = 242 ml	
Formulation 9	V0 = 285 ml	7.4
	V10 = 270 ml	
	V50 = 258 ml	
	V500 = 250 ml	
Formulation 10	V0 = 250 ml	3.87
	V10 = 232 ml	
	V50 = 225 ml	
	V500 = 223 ml	
Formulation 11	V0 = 290 ml	6.25
	V10 = 272 ml	
	V50 = 260 ml	
	V500 = 255 ml	
Formulation 13	V0 = 235 ml	6.66
	V10 = 225 ml	
	V50 = 215 ml	
	V500 = 210 ml	

This table shows that, as for their ability to compact, for all the tests, the values found do not exceed 20ml, and their Carr indices are all less than 18%.

3.3.3. Results of friability

friability test evaluates the resistance of the tablets to wear and crumbling during handling and transport. The tablets are placed in a rotating drum where they are subjected to mechanical shocks. After a set number of rotations, the tablets are weighed to measure mass loss. A brittle rate of less than 1% is generally considered acceptable. This test is crucial to ensure the physical integrity and quality of the tablets throughout their life cycle.

Table XI The friability results

Formulations	**Results (%)**
Formulation 01	0.79

Formulation 03	0.426
Formulation 4	0.76
Formulation 7	0.69
Formulation 8	1.02
Formulation 9	\
Formulation 10	0.96
Formulation 11	0.25
Formulation 12	0.69
Formulation 13	0,69

This table represents the friability test results and it is noted that only one lot (lot 008) is not in the standards is greater than 1 (1.02), and we noticed the (lot 9) is so crumbly

3.3.4. Results of Hardness

hardness test measures the force required to break a tablet, thus evaluating its resistance to pressure. This test is performed by applying increasing pressure until the tablet fractures. The optimal hardness ensures that the tablets are robust enough to withstand handling and transport while being brittle enough to disintegrate and dissolve properly in the body. Proper hardness is essential to ensure the quality, efficacy, and consistency of pharmaceutical tablets.

Table XII Hardness test results

Samples	**Results (Neoten)**
Formulation 01	56.01
Formulation 3	95.45
Formulation 4	71.05
Formulation 7	53.72
Formulation 8	47.67
Formulation 9	12.59
Formulation 10	49.64

Formulation 11	30.5
Formulation 12	30
Formulation 13	66

This table shows the obtained results from the hardness test of the tablets for the purpose of compression, it should be noted that batch 3 has a higher bearing power than the other batches (95.45N) so it is hard than the other batches. Unlike in formulation 9 the power is (12.59N) so it is not hard like the others.

3.3.5. Results of average weight

In this test, 20 tablets from each batch are measured, the average is calculated, and the obtained results is in the table below.

Table XIII Results of the average weight of 20 tablets in each batch

Samples	**Results (Grams)**
Formulation 1	1.201
Formulation 3	1.201
Formulation 4	1.199
Formulation 7	1.208
Formulation 8	1.193
Formulation 9	1.180
Formulation 10	1.211
Formulation 11	1.220
Formulation 12	1.194
Formulation 13	1.194

This table shows the obtained results after weighing 20 tablets in each batch and calculating the average of each batch and it can be seen that the weight of tablets is approximately 1.2 grams in all batches within a range of 0.30%.

3.3.6. Thickeness

The thickness of 20 tablets is measured and the average of the diameters is calculated.

Table XIV Results of thickeness

Samples	**Results (mm)**
Formulation 1	5.825
Formulation 3	5.545
Formulation 4	5.721
Formulation 7	5.767
Formulation 8	5.761
Formulation 9	5.2
Formulation 10	6
Formulation 11	6.036
Formulation 12	5.805
Formulation 013	5.801

This table represents the measurement results of the diameter of the 20 tablets, we notice that there is a variation in the diameters of tablets.

3.4. Test of dissolution of tablets

Using an ARMFIELD brand dissolutest in the three pH ranges (pH 1.2, pH 4, pH 5.8) and usin visible UV at $\lambda = 268$ nm, the absorbance and yield are measured in each batch (Formulation 1,3,4,7,10,13) and each range.

Remark

This obtained results for some dissolutest vases were aberrant, because there was a problem with them, which is why we eliminated the profiles drawn from these results.

Medium 1: pH 1.2

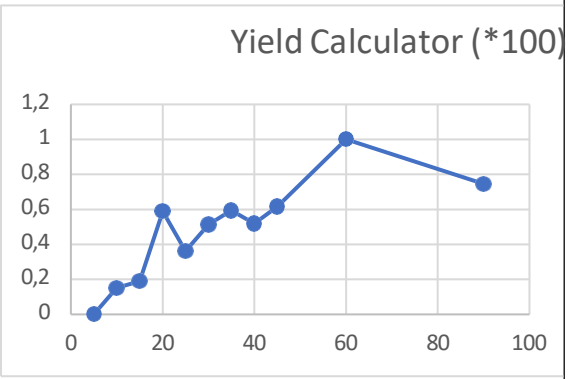


FIGURE 12 Release of the active substance versus time for formulation 1 at pH 1.2

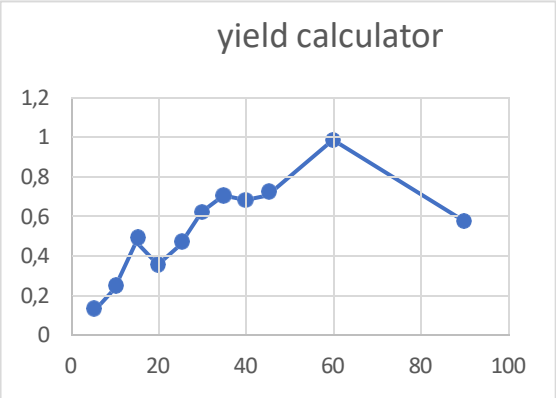


FIGURE 13 Release of the active substance versus time for formulation 3 at pH 1.2

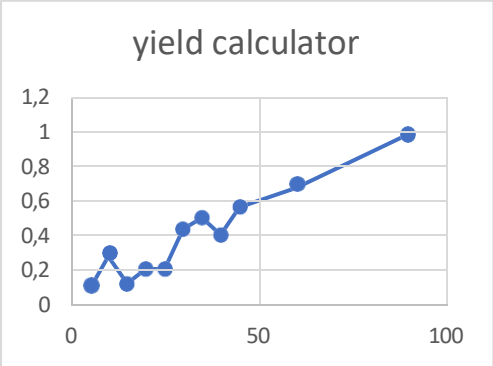


FIGURE 14 Release of the active substance versus time for formulation 4 at pH 1.2

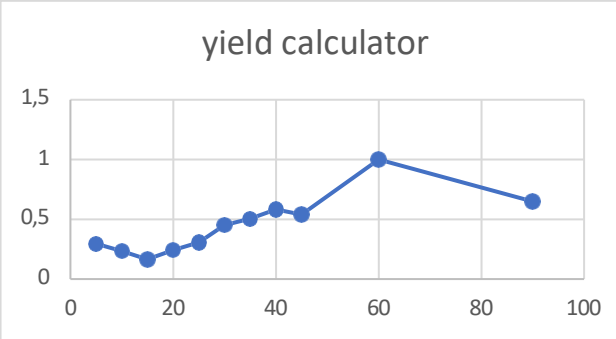
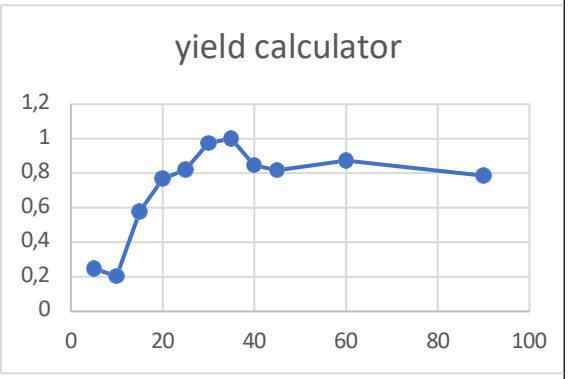


FIGURE 15 Release of the active substance versus time for formulation 7 at pH 1.2



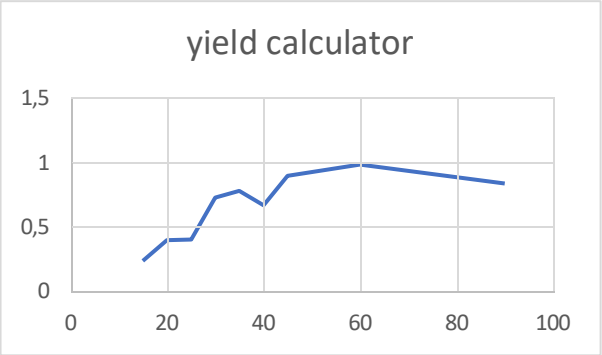


FIGURE 17 Release of the active substance versus time for formulation 13 at pH 1.2

FIGURE 16 Release of the active substance versus time for formulation 10 at pH 1.2	

This obtained results from the test of dissolution of tablets in an acidic medium (pH: 1.2) show that, the dissolution completes of the tablets in 60 min (100% yield) and after the 60 min the yield is decrease in the batches (1,3,7,13):

In the vase 4: we noticed that the dissolution completes of tablet in 90 min

vase 10: we noticed that the dissolution completed in 35 min and after that the yield decreased.

second medium: pH 5.8

results of dissolution in pH 5.8 are given in the following curves.

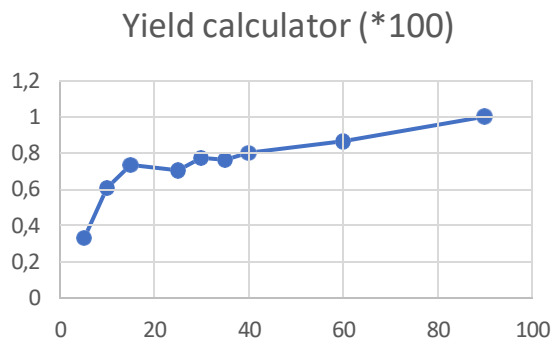


FIGURE 18 Release of the active substance versus time for formulation 1 at pH 5.8

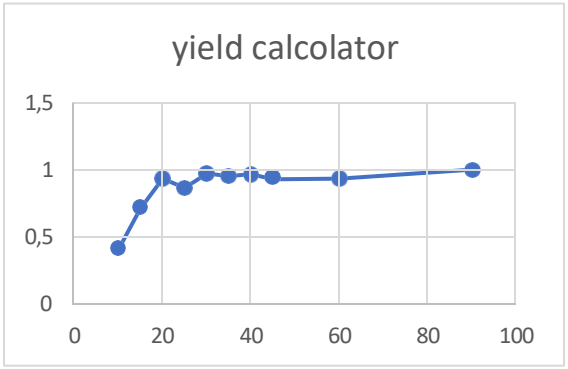
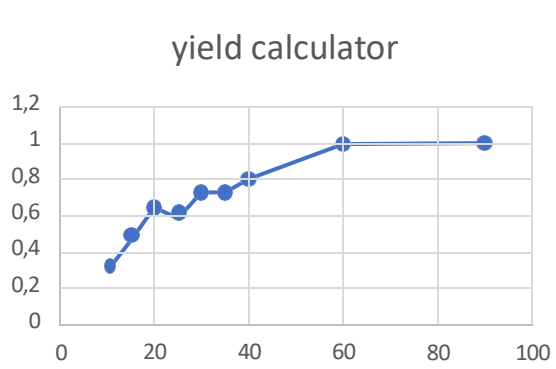


FIGURE 19 Release of the active substance versus time for formulation 3 at pH 5.8



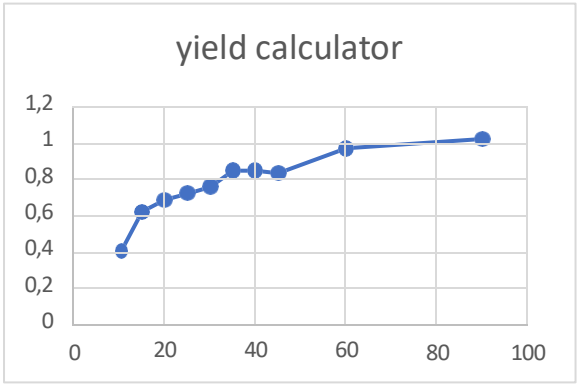
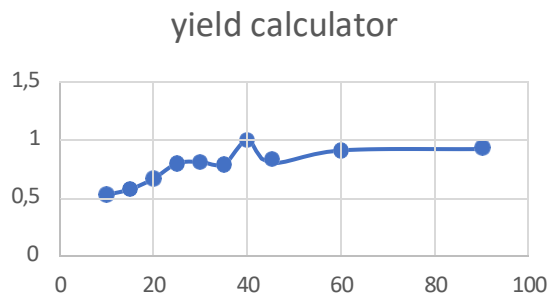
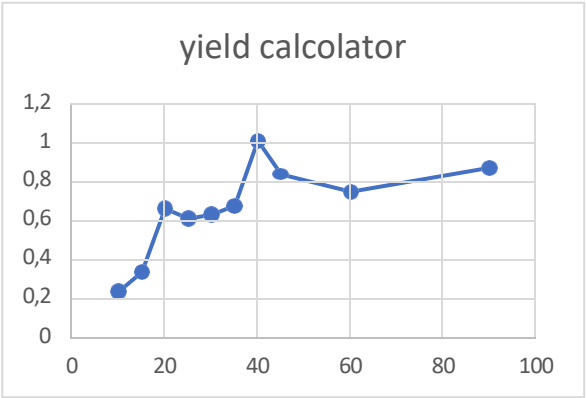


FIGURE 20 Release of the active substance versus time for formulation 4 at pH 5.8	**FIGURE 21** Release of the active substance versus time for formulation 7 at pH 5.8
 **FIGURE 22** Release of the active substance versus time for formulation 10 at pH 5.8	 **FIGURE 23** Release of the active substance versus time for formulation 13 at pH 5.8

This table shows the obtained results from the test of dissolution of tablets in an acidic medium (pH: 5.8) using a visible UV spectrophotometer.

In batches (1,3,4,7): we notice that the dissolution complete of the tablets in 90 min (100% yield)

batches 10 and 13: we noticed that the dissolution completed in 40 min and after that the yield decreased.

medium pH= 4

results of dissolution in pH 4 are given in the following curves.

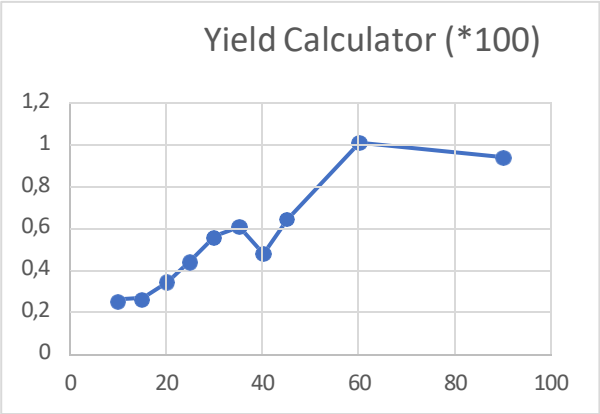


FIGURE 24 Release of the active substance versus time for formulation 1 at pH 4

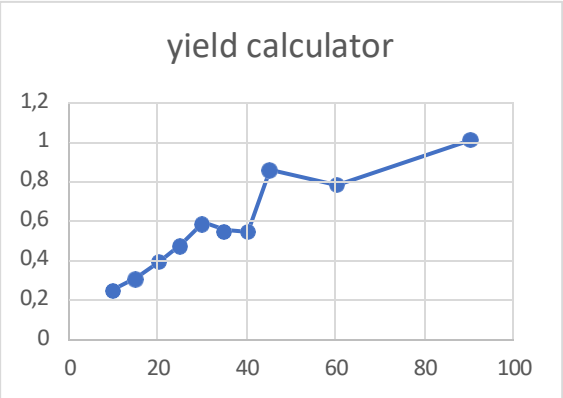


FIGURE 25 Release of the active substance versus time for formulation 1 at pH 3

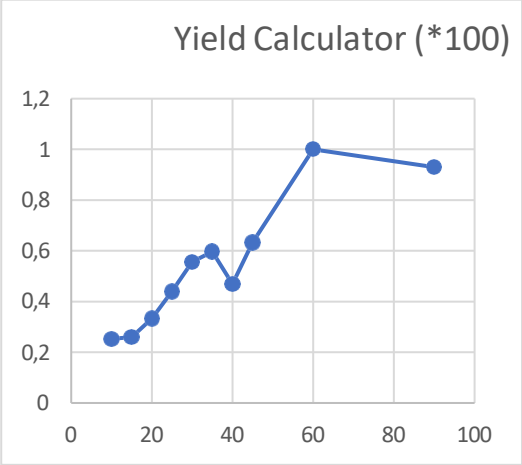


FIGURE 26 Release of the active substance versus time for formulation 1 at pH 4

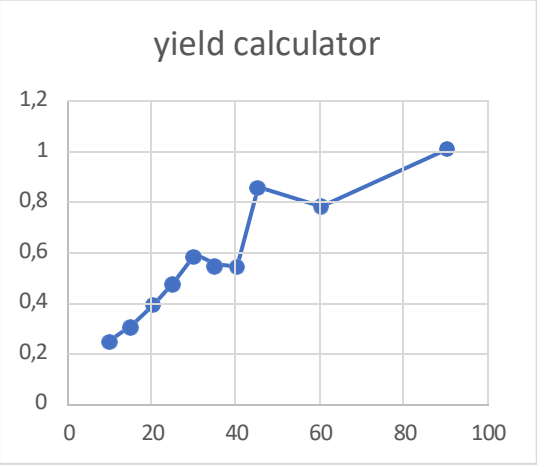


FIGURE 27 Release of the active substance versus time for formulation 3 at pH 4

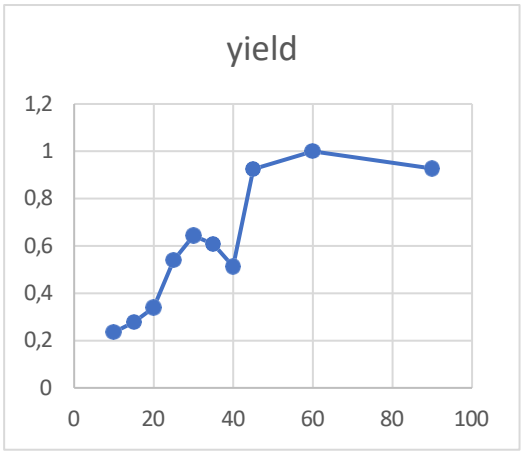


FIGURE 28 Release of the active substance versus time for formulation 4 at pH = 4

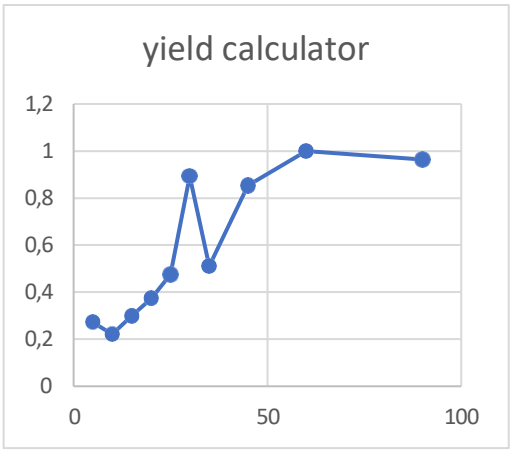


Figure 29 Release of the active substance versus time for formulation 7 at pH = 4

These results can be explained as follows:

The average dissolution curves of the majority of tests resemble conventional release.

The tablets obtained at the end of the 16 tests release 50% of their active ingredient after, 5 min and after 60 min we obtain 100% of release.

In addition to obtained results above, it is possible to provide comments relating to the physical and kinetic interpretation of the latter.

Indeed, the release of the active ingredient through a hydrophilic matrix takes place in several stages:

Upon first contact with digestive fluids, a small fraction of the active substance is possibly dissolved quickly.

Then the progressive penetration of the solvent allows the hydration of the system and the gelation of the macromolecules, which constitute an increasingly thick viscous layer from which the medicinal substance is released after dissolution and diffusion through the gel.

In such a system, where the active substance is simply dispersed in a polymeric support, it is the swelling of the HPMC which controls the release by formation of a gelled layer accompanied by a slight erosion of the tablet.

3.5. RESPONSE SURFACE MODELING

Modelling parameters were presented as response surfaces

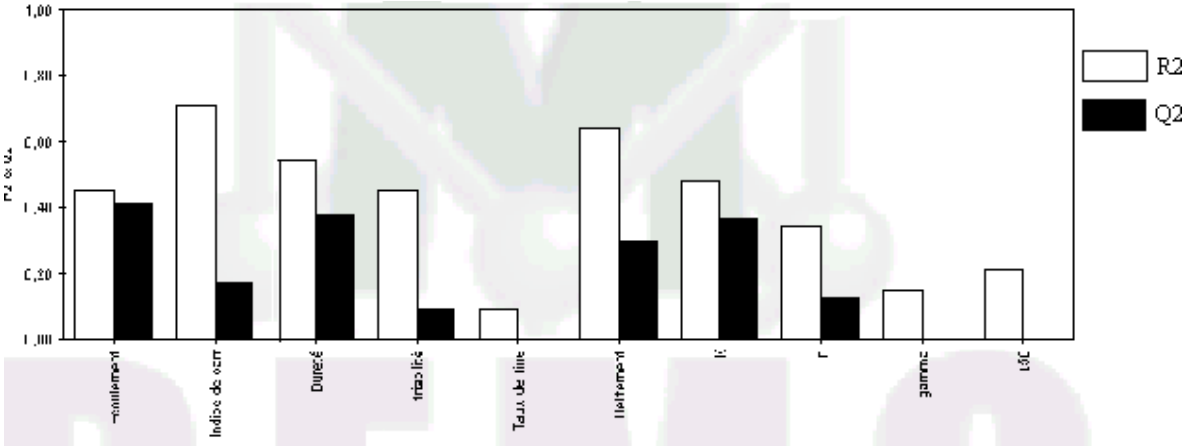


Figure 30 Response Surface Histogram

effectiveness of the MODDE 6 model is based on the following parameters:

• R 2: Correlation coefficient, explains the percentage of the variance. It must be greater than 70%.

- Q 2: Prediction coefficient

• Validity of the model

• Model reproducibility the descriptive (R2) and predictive (Q2) qualities of each model are provided in the histogram above.

It should be noted that these results could only be obtained after excluding certain aberrant trials.

We see that the values of the coefficient of determination R2 are high practically for all the answers, with the exception of answer b. So, in light of these results, we can say that these values demonstrate the good descriptive quality of our models. As for the values of the prediction coefficients are much less interesting; they are 50% lower for most responses. So the models do not have better predictive qualities for all answers.

3.6. Determination of optima

By introducing the target values of the responses, characteristics of the reference product, into the MODDE 6 software, we then obtain a set of optima (8 optima) presented in table IV.23 below.

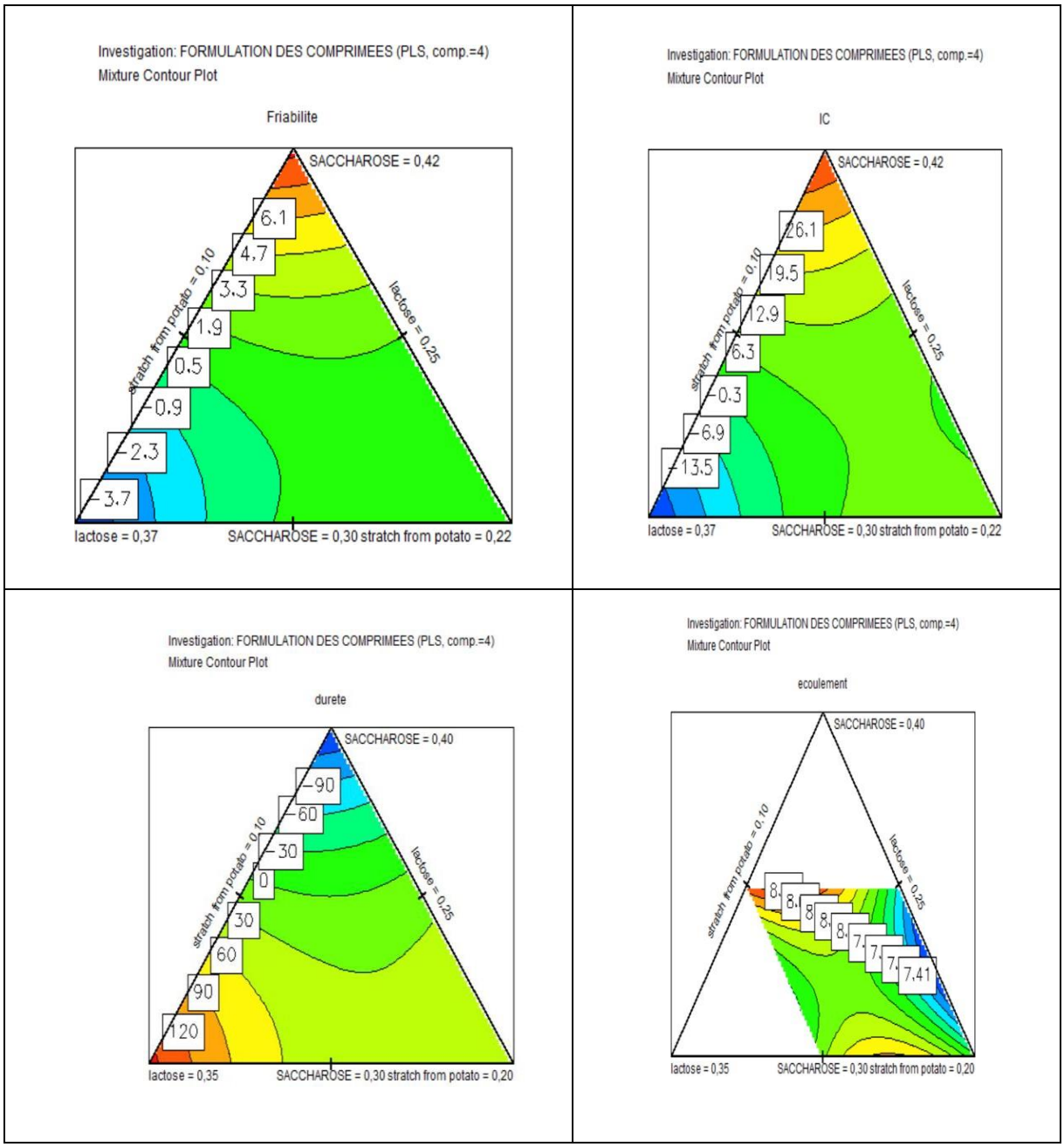


Figure 31 optima results

In this context, an optimum was identified formulation 3, achieved and validated experimentally and statistically. Thus, the tablet produced on a laboratory scale complies with the standards required by the pharmacopoeias.

ANNEXE

Using an ERWEKA brand dissolute in the 3 pH ranges (pH 1.2, pH 4, pH 5.8) and visible UV the absorbance and yield are measured in each batch (LOT1,3,4,7,10,13) and each range,

Medium 1: pH 1.2

TABLE XV results obtained from the test of dissolution of tablets in an acidic medium (Ph:1.2)

Yield Calculator (*100)	Comments	WL265,0
0.0001	Lot 01 05min	0.029

0.1513	Lot 01 10min	0.028
0,1891	Lot 01 15min	0.035
0.5891	Lot 01 20min	0.109
0.3621	Lot 01 25min	0.067
0.5135	Lot 01 30min	0.095
0.5945	Lot 01 35min	0.110
0.5189	Lot 01 40min	0.096
0.6162	Lot 01 45min	0.114
1	Lot 01 60min	0.185
0.7459	Lot 01 90min	0.138
0.1244	Lot 03 05min	0.027
0.2442	Lot 03 10min	0.053
0.4838	Lot 03 15min	0.105
0.3686	Lot 03 20min	0.080
0.4654	Lot 03 25min	0.101
0.6359	Lot 03 30min	0.138
0.7188	Lot 03 35min	0.156
0.6958	Lot 03 40min	0.151
0.7188	Lot 03 45min	0.156
1	Lot 03 60min	0.217
0.5898	Lot 03 90min	0.126
0.1034	Lot 04 05min	0.024
0.2931	Lot 04 10min	0.068
0.1379	Lot 04 15min	0.032
0.2198	Lot 04 20min	0.071
0.2198	Lot 04 25min	0.071
0.4525	Lot 04 30min	0.105

0.5172	Lot 04 35min	0.120
0.4181	Lot 04 40min	0.097
0.5775	Lot 04 45min	0.134
0.6896	Lot 04 60min	0.160
1	Lot 04 90min	0.232
0.296	Lot 07 05min	0.061
0.2330	Lot 07 10min	0.048
0.1650	Lot 07 15min	0.034
0.2427	Lot 07 20min	0.050
0.3058	Lot 07 25min	0.063
0.4514	Lot 07 30min	0.093
0.5048	Lot 07 35min	0.104
0.5825	Lot 07 40min	0.120
0.5388	Lot 07 45min	0.111
1	Lot 07 60min	0.206
0.6504	Lot 07 90min	0.134
0.2491	Lot 10 05min	0.071
0.2035	Lot 10 10min	0.058
0.5789	Lot 10 15min	0.165
0.7684	Lot 10 20min	0.219
0.8210	Lot 10 25min	0.234
0.9754	Lot 10 30min	0.278
1	Lot 10 35min	0.285
0.8456	Lot 10 40min	0.241
0.8175	Lot 10 45min	0.233
0.8736	Lot 10 60min	0.249
0.7859	Lot 10 90min	0.224

0.2947	Lot 13 05min	0.084
0,0561	Lot 13 10min	0.016
0.2526	Lot 13 15min	0.072
0.4140	Lot 13 20min	0.118
0.4175	Lot 13 25min	0.119
0.7438	Lot 13 30min	0.212
0.7964	Lot 13 35min	0.227
0.6842	Lot 13 40min	0.195
0.9122	Lot 13 45min	0.260
1	Lot 13 60min	0.285
0.8526	Lot 13 90min	0.243

Table XVI results obtained from the test of dissolution of tablets in an acidic medium (Ph:5.8)

Yield calculator (*100)	Comments	WL265,0
0.3203	lot 1 10min	0.066
0,6067	lot 1 15min	0.125
0.7330	lot 1 20min	0.151
0.7330	lot 1 25min	0.151
0.7038	lot 1 30min	0.145
0.7718	lot 1 35min	0.159
0.7621	lot 1 40min	0.157
0.8009	lot 1 45min	0.165
0.1359	lot 1 05min	0.028
0.8640	lot 1 60min	0.178
1	lot 1 90min	0.206
0.4029	lot 3 10min	0.083
0.7087	lot 3 15min	0.146

0.9320	lot 3 20min	0.192
0.8640	lot 3 25min	0.178
0.9708	lot 3 30min	0.200
0.9514	lot 3 35min	0.196
0.9660	lot 3 40min	0.199
0.9271	lot 3 45min	0.191
0.2038	lot 3 05min	0.042
0.9320	lot 3 60min	0.192
1	lot 3 90min	0.206
0.2955	lot 4 10min	0.060
0.4630	lot 4 15 min	0.094
0.6453	lot 4 20 min	0.131
0.5862	lot 4 25min	0.119
0.7290	lot 4 30min	0.148
0.7290	lot 4 35min	0.148
0.8029	lot 4 40min	0.163
0.2758	lot 4 5min	0.056
0.9950	lot 4 60min	0.202
1	lot 4 90min	0.203
0.3632	lot 7 10min	0.077
0.5990	lot 7 15min	0.127
0.6650	lot 7 20min	0.135
0.6981	lot 7 25min	0.148
0.7358	lot 7 30min	0.156
0.8254	lot 7 35min	0.175
0.8255	lot 7 40min	0.187
0.8113	lot 7 45min	0.172

0.2877	lot 7 5min	0.061
0.9481	lot 7 60min	0.201
1	lot 7 90min	0.212
0.5294	lot 10 10min	0.180
0.5764	lot 10 15min	0.196
0.6676	lot 10 20min	0.277
0.8	lot 10 25min	0.272
0.8117	lot 10 30min	0.276
0.7911	lot 10 35min	0.269
1	lot 10 40min	0.340
0.8029	lot 10 45min	0.273
0.2058	Lot 10 5min	0.070
0.9117	lot 10 60min	0.310
0.9235	lot 10 90min	0.314
0.224	lot 13 10min	0.084
0.3253	lot 13 15min	0.122
0.6506	lot 13 20min	0.244
0.6	lot 13 25min	0.255
0.6186	lot 13 30min	0.232
0.666	lot 13 35min	0.250
1	lot 13 40min	0.375
0.8266	lot 13 45min	0.310
0.0000	Lot 13 5min	0.001
0.7386	lot 13 60min	0.277
0.8613	lot 13 90min	0.323

The third medium: pH 4

Table XVII results obtained from the test of dissolution of tablets in an acidic medium (Ph:4)

Yield Calculator (*100)	time (min)	Wl (265)
0,2527	10 min 01	0.069
0,26	15 min 01	0.071
0,3333	20 min 01	0.091
0,4395	25 min 01	0.120
0,4688	40 min 01	0.128
0,5567	30 min 01	0.152
0,597	35 min 01	0.163
0,6336	45 min 01	0.173
0,9304	01h30 01	0.254
1	01h 01	0.273
0,2467	10 min 03	0.076
0,3051	15 min 03	0.094
0,3831	20 min 03	0.118
0,474	25 min 03	0.146
0,5357	40 min 03	0.165
0,5454	35 min 03	0.168
0,5844	30 min 03	0.180
0,7727	60 min 03	0.238
0,8506	45 min 03	0.262
1	90 min 03	0.308
0,2352	10 min 04	0.072
0,2777	15 min 04	0.085
0,3398	20 min 04	0.104
0,5130	40 min 04	0.157
0,5392	25 min 04	0.165
0,6078	35 min 04	0.186
0,6437	30 min 04	0.197

0,9248	45 min 04	0.283
0,9281	01h30 04	0.284
1	01h 04	0.306
0,2214	10 min 07	0.062
0,2714	5 min 07	0.076
0,3	15 min 07	0.084
0,3714	20 min 07	0.104
0,475	25 min 07	0.133
0,5107	35 min 07	0.143
0,8535	45 min 07	0.239
0,8928	30 min 07	0.250
0,9642	01h30 07	0.270
1	01h 07	0.280

General conclusion

We can conclude our End-of-Studies Project to develop a syrup and tablets based on Asparagus officinalis by highlighting the success of the formulation of these two products while maintaining the pharmacological properties of the plant, known for its diuretic, anti-inflammatory, antioxidant and immunomodulatory effects. The project rigorously employed extraction techniques such as vacuum maceration and evaporation, as well as quality testing, including rheology, pH and compressibility tests, to ensure the stability and efficiency of the finished products. The results confirmed that the formulations developed meet pharmaceutical standards and offer an effective natural alternative to synthetic drugs, especially for children and the elderly thanks to the syrup form, and for a wider population with the tablets. This project highlights the potential of medicinal plants for the development of new dosage forms, opening up prospects for future research and applications in natural medicine. In conclusion, the success of this project in creating stable and effective formulations from Asparagus officinalis demonstrates a significant advance in pharmacotoxicology, offering natural therapeutic solutions that meet current public health needs

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