DEVELOPMENT OF TECHNOLOGY FOR OBTAINING IMMUNE-STIMULATING SUBSTANCES BASED ON MEDICINAL PLANTS

Jabborova Shahzoda Abdulla qizi

Abdug'afforov Abbosxo'ja Abdulla og'li

Scientific supervisor: To'xtayev Farxod Xakimovich

Tashkent Pharmaceutical Institute,

Tashkent, Uzbekistan.

Abstract Medicinal plants have been widely used to treat a variety of infectious and non-infectious ailments. According to one estimate, 25% of the commonly used medicines contain compounds isolated from plants.

Keywords: Medicinal plants; Traditional medicine; Viral infections; Antivirals.

Абстракт Лекарственные растения широко используются для лечения различных инфекционных и неинфекционных заболеваний. Согласно одной оценке, 25% широко используемых лекарств содержат соединения, выделенные из растений.

Ключевые слова: Лекарственные растения; Традиционная медицина; Вирусные инфекции; Противовирусные препараты.

The history of medicinal plants dates back to the origin of human civilization on earth. Several of these may have been used to treat viral infections in the past, however, first recognized interest in their development as antiviral agent is the efforts of the Boots drug company to screen 288 plants for anti-influenza activity. Later studies have reported the inhibitory effects of medicinal plants extracts on the replication of several viruses. Particularly herpes simplex virus type 2 (HSV-2), HIV, hepatitis B virus (HBV) , and emerging viral infections associated with poxvirus and severe acute respiratory syndrome (SARS) virus were strongly inhibited by various plants extracts. Most of these studies have utilized either water soluble or alcoholic extracts of medicinal plants, and limited efforts have been directed toward the identification of active natural ingredient exhibiting antiviral effects. Moreover, recent studies showing antiviral potential of plant extracts against viral strains resistant to conventional antiviral agents have challenged the modern drug discovery practices, and deem a very careful look toward exploring natural antiviral components of medicinal plants.

The very first and basic step towards evaluating the therapeutic potential of a medicinal plant is preparation of crude cellular lysate of the plant matrix followed by extraction of various components having potential medicinal value. There are several books and reviews describing standardized extraction procedures from medicinal plants. A few to start with could be: Plant Drug Analysis: A Thin Layer Chromatography Atlas , Modern Phytomedicine: Turning Medicinal Plants into Drugs and Laboratory Handbook for the Fractionation of Natural Extracts. Most of the books published in phytomedicine have mainly paid attention to classical isolation procedures. Unfortunately, some of these classical procedures have limitations of reproducibility and quality, thus compromising the safety and efficacy of phytomedicinal preparations. As such there is an urgent need to refine and further develop classical methodologies to obtain procedural consistency and highly pure plant components exhibiting medicinal value. In recent past, increased interest in traditional medicine has complemented quality awareness and refinement in extraction methodologies and standardization of procedures for phytochemedicinal products isolation . To ensure high quality herbal preparations, efforts are ongoing to replace traditional methodologies with modern sample preparation and extraction procedures. Classical solvent separation of phytomedicinal products is being complemented with modern techniques like microwave-assisted extraction, pressurized liquid extraction, matrix-assisted laser desorption/ionization mass spectrometry and several others. To further facilitate plant-based drug discovery efforts are also being directed toward standardization of methodologies which can be used to study pharma cokines /pharmacodynamics behavior of phytomedicinal products . Chamomile has been used for centuries as a medicinal plant mostly for its anti-inflammatory, analgesic, anti-microbial, antispasmic and sedative properties. As a member of compo site family, it is widely represented by two known varieties viz. chamomile (Matricaria chamomilla) and Roman chamomile (Chamaemelum nobile). Chamomile in particular is the most common variety used for medicinal purposes . In fact, infusion is one of the most popular methods and has been traditionally used as carminative and mild sedative to calm nerves and reduce anxiety, to treat hysteria, nightmares, insomnia and other sleep problems. Additionally, chamomile has been valued as a digestive relaxant and has been used to treat various gastrointestinal disturbances including flatulence, indigestion, diarrhea, anorexia, motion sickness, nausea, and vomiting . The widespread use and medicinal properties has made chamomile increasingly popular in the form of tea which is consumed at a rate of over one million cups per day. Apart from the existing traditional knowledge on its therapeutic efficacy more work has been conducted in recent years on chamomile to establish its antioxidant,

For agent/drug development, information about stability of the product over the period of time and the effect of ambient temperature and other geophysical conditions, the duration which retains the acceptable limit of efficacy and quality is designated as the shelf-life or keeping quality. For such studies, both aqueous and methanolic chamomile extracts were aliquot from the freshly prepared extract and transferred in 1.5 ml eppendorf tubes. These tubes were distributed in 3 groups to store at −20°C, 4°C and at room temperature. The tubes were retracted at 15, 30, 60, 90 and 120 days for analysis and dissociation of glucoside bond and were also subjected to efficacy assessment by MTT assay to assess the anti-proliferative efficacy in human prostate cancer PC-3 cells. In addition, we performed stability studies on aqueous and methanolic chamomile extracts at different pH, light exposure and long term storage.

The major phytochemicals in flowers, leaves, and stem of salvia officinalis are well identified. A wide range of constituents include alkaloids, carbohydrate, fatty acids, glycosidic derivatives (e.g., cardiac glycosides, flavonoid glycosides, saponins), phenolic compounds (e.g., coumarins, flavonoids, tannins), poly acetylenes, steroids, terpenes/terpenoids (e.g., monoterpenoids, diterpenoids, triterpenoids, sesquiterpenoids), and waxes are found in salvia officinalis. Structure of main flavonoids and terpenes/terpenoids isolated from salvia officinalis is shown, respectively. Most of the phytochemicals which are reported from salvia officinalis have been isolated from its essential oil, alcoholic extract, aqueous extract, butanol fraction, and infusion preparation. More than 120 components have been characterized in the essential oil prepared from aerial parts of salvia officinalis. The main components of the oil include borneol, camphor, caryophyllene, cineole, elemen, humulene, ledene, pinene, and thujone. Alcoholic and aqueous extracts of salvia officinalis are rich in flavonoids particularly rosmarinic acid and luteolin-7-glucoside. Also the phenolic acids such as caffeic acid and 3-Caffeoylquinic acid have been found in methanolic extract of salvia officinalis. Several flavonoids like chlorogenic acid, ellagic acid, epicatecin, epigallocatechin gallate, quercetin, rosmarinic acid, rutin, and luteolin-7-glucoside, as well as several volatile components such as borneol, cineole, camphor, and thujone have been identified in infusion prepared from salvia officinalis. Rosmarinic acid and ellagic acid are the most abundant flavonoids in S. officinalis infusion extract, followed by rutin, chlorogenic acid, and quercetin. The most abounding carbohydrates described in this plant are arabinose, galactose, glucose, mannose, xylose, uronic acids and rhamnose.

Rosemary (Rosmarinus officinalis Linn. Family Labiatae) is a perennial plant native of the Mediterranean area. Rosemary extracts are used routinely for cooking, preservation of foods, cosmetics, or in herbal medicine for anti-inflammatory and antimicrobial applications , and for the prevention and treatment of diabetic and cardiovascular diseases . At least 30 components have been identified in essential oils, which have been shown to possess olfactory properties that influence cognitive performance including memory. Rosemary extracts contain many bioactive components including phenolic mono-terpenes (α-pinene, camphene, limonene) , diterpenes (carnosic acid, carnosol), flavones (genkwanin, isoscutellarein 7-O-glucoside), and caffeolyl derivatives (rosmarinic acid). The highest accumulation of these groups of compounds occurs in leaves and it is related to young stages of plant development . In general, rosmarinic acid is present at the highest concentration in all rosemary plant organs. Carnosic acid and carnosol are found in stems during young stages, but their concentrations decrease in the vascular system following aging. However, high levels of phenolic diterpenes and rosmarinic acid are found in flowers as a result of in situ biosynthesis and transport from other plant organs. Rosemary extracts in both aqueous and lipid medium have been shown to possess antioxidant activity, which is due to the presence of a catechol group in the aromatic ring of the phenolic terpenes, and cathecols conjugated with a carboxylic acid group in rosmarinic acid. Interestingly, rosmarinic acid is more effective as antioxidant in bulk oil whereas carnosol and carnosic acid perform better in oil-in-water emulsions. These differences in antioxidant efficacy have been attributed to interfacial partitioning of these compounds .

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