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Full Length Research Paper

Medicinal properties of *Commiphora gileadensis*

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***Commiphora gileadensis* is a plant that was cultivated in ancient times in the land of Israel, particularly in the oases of the Dead Sea Basin — Ein Gedi and Jericho. The plant, also known as balsam, was renowned for the expensive perfume that was produced from it, as well as for exceptional medicinal properties that were attributed to its sap, wood, bark, and seeds. This article presents the historical sources describing these health-related properties and preliminary laboratory studies demonstrating the pharmacological effects of balsam sap. Investigations of the antimicrobial activity of *C. gileadensis* showed the plant sap inhibitory effect against *Bacillus cereus* and the blocking of *Pseudomonas aeruginosa* lectins. These results corroborate the historical sources crediting the usefulness of balsam sap as an antiseptic agent.**

Key words: *Commiphora gileadensis*, balsam, resin, perfume, antimicrobial effects.

INTRODUCTION

Commiphora gileadensis (syn. *Commiphora opobalsamum*) is a tree in the *Burseraceae* family. There are those who identify this plant with the "balm" or "balsam" mentioned in translations of the Bible (Genesis 37:25; 43:11; Jeremiah 46:11, 8:22).

The balm of Judea was described in the Hellenistic and Roman-Byzantine periods as the world's most well-known and expensive perfume. It was recognized by all of the ancient writers – Jewish, as well as Greek and Roman (Feliks, 1995; Stern, 1974-1984) – and its existence and use were also reported in the archeological literature (Amar, 2002; Hepper and Taylor, 2004). The perfume was widely known in the Mediterranean Basin because balsam was cultivated exclusively in the land of Israel or, more precisely, in the oases of the Dead Sea Basin, Ein Gedi and Jericho. It was recognized in ancient times, along with myrrh and frankincense, as a perfume and incense plant that grows in areas with very specific ecological conditions (Groom, 1981). In the Middle Ages, balsam cultivation shifted to Egypt for approximately one thousand years (Milwright, 2001, 2003), but its importance has declined over the last few centuries.

Different proposals have been offered for the identity of balsam (Löw, 1967; Moldenke and Moldenke, 1952). However, from as early as the sixteenth century until modern times, researchers (Alpini, 1718; Feliks, 1995; Hepper, 1992; Linnaeus, 1764) have agreed with confidence that balsam is *Commiphora gileadensis*[1] (=*C. opobalsamum*), which grows wild today in the dry stony hills around the Red Sea, and especially within the borders of Saudi Arabia, Yemen, Oman, and Eritrea (Miller and Morris, 1988; Wood, 1997).

We briefly survey ancient and more recent accounts of the medicinal uses of balsam, and report on the bacteriological and biochemical tests that we carried out on the

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[1] In English it is called by several names: balsam of Mecca, balm of Gilead. It is possible that the name balsam also includes the species *Commiphora kataf*, but we will not deal with that here.

plant's sap confirm, in principle, the historic records.

EARLY ACCOUNTS ON BALSAM

The medicinal uses of balsam are mentioned frequently in the classical sources – probably an offshoot of its fame as a widely used perfume component. It was claimed to have been used for the treatment of almost all human diseases. Diodorus (1961) and Tacitus (1956) described balsam in general terms as a medicinal factor and mentioned its importance to physicians (Diodorus of Sicily, 1961; Tacitus, 1956). Galen (131-200 CE) listed it among the world's finest drugs. The balsam of Judea (*Apobalsami Iudaicae*) is also mentioned in Mulomedicina Chironis (Mule-therapy by Chiron), an anthology of medicines for veterinary use compiled in the second half of the fourth century (Stern, 1974-1984).

All parts of the balsam plant were used in medicine, and Pliny (1989) noted that even the bark was sold for making drugs. Its sap (also called a resin) was particularly known for its ability to cure headaches, early-stage cataract, and blurred vision (Largus, 1887; Strabo, 1961). Oil containing balsam sap was considered of prime value in preparing medicinal ointments and compresses, and its other parts (bark, wood, and seeds) were used in various drugs (Celsus, 1961; Largus, 1887). Preparations containing the sap were considered to be effective in the treatment of hearing disorders, paralysis, stroke, and in mending fractures. Small doses of resin were recommended, because an excess could aggravate an illness (Pliny, 1989). Balsam was also used as a diuretic drug, as a cure for respiratory diseases and coughing, and as an anti-toxin – acting as a snake-bite antidote (Gunther, 1959; Largus, 1887). In addition, it was also used in the field of traditional gynecology for the treatment of cervical infections and for delaying menstruation (Gunther, 1959). Applying balsam sap to the opening of the cervix before sexual relations was believed to act as a contraceptive (Temkin, 1991).

The Rabbinic literature mentions a tonic known as "*aluntis*," which was composed of old wine mixed with clear water and balsam. It was drunk in the bathhouse after bathing as a cooling beverage or to anoint and strengthen the body (Talmud Bavli, 1997). In his treatise, the physician Assaph ha-Rofe (ca. 8-9th centuries) referred to diverse medicinal uses of balsam. However, most of his information was derived from the classical medical literature (primarily Disocorides), and he ended his extensive survey with the statement, "Give to drink [of this tonic] for all illnesses and it will cure them, and it will eliminate also every ache that may be in the stomach and bowels, and in most cases it will bring cures" (Muntner, 1969).

Balsam is also mentioned in the pharmacological literature of the Middle Ages (Muntner, 1949) as an off-the-shelf drug that should be kept by all pharmacists (Saladino di Ascoli, 1953). Qusta Ibn Luqa (end of the 9th century) mentioned the treatment of ear aches stemming from common colds with drops of "balsam" oil (Bos, 1992). The oil was also recommended as a therapy for epilepsy, as found in the book of Rabbi Hayim Vital (1543-1620), "For the falling sickness: If you anoint his nose with 'balsamo' oil, the illness will be at rest for 15 or 20 days and will not afflict him" (Buchman and Amar, 2006). Most of the more recent historic medical treatises merely repeated the information of the ancient sources. This helps to explain how Greek medical tradition continued down to the Middle Ages (Ibn al-Baytar, 1874).

The transfer of medical knowledge is also reflected by recorded practice. Balsam was traded together with other medicinal and perfume components and was included in medical prescriptions, as documented in the Cairo Geniza of the mid-11th century (T-S Ar.34.34; T-S Ar.34.305). Pharmacists would peel the branches and sell the bark for "heating the body" (see below) or they would press the wood and sell the extracted substance (al-Biruni, 1973). During the Mamluk Period, balsam oil was sent from Egypt to the hospitals of Syria for patients suffering from "cold" diseases, namely backache, knee pain, and catarrh (excessive phlegm), as recounted by Ibn Fadlallah al-'Umari (1301-1349) (al-Umari, 1985).

Two of the most famous uses of balsam were for treating injuries and tissue healing (Ludolph Von Suchem, 1890). Balsam oil extracted by boiling twigs in water was reported to be effective for treating skin infections and wounds, and especially against traumatic injuries and fractures, such as those caused by falling from high places (Ludolph Von Suchem, 1890; Benajahu, 1985). The plant was also credited with improving memory and digestion (Benajahu, 1985).

STUDIES ON THE MEDICINAL USES OF *COMMIPHORA GILEADENSIS*

C. gileadensis is no longer a factor in modern applications of traditional drugs except for its negligible exploitation by populations living close to wild habitats where it is found. Various medicinal products are made from the plant by Semitic tribes in the Dhofar region of Oman. For example, the inside of the dried bark is placed on wounds as an antiseptic agent, while a tincture of ground balsam bark is used to treat skin diseases such as inflammations and eczema. It has also been attributed as being a cure for rabies, to alleviate labor pains, and as being useful in bathing newborn babies (Miller and Morris, 1988).

Abdul-Ghani and Amin (1997) used an aqueous extract of *C. gileadensis* branches as an antihypertensive. The intravenous administration of 4 mg/kg of the balsam extract to anaesthetized rats depressed systemic arterial blood pressure by 20% ($P < 0.01$) and reduced their heart rate by 14% ($P < 0.05$). The hypotensive and bradycardiac effects were immediate and expressed in a dose-dependent manner. The authors have suggested that the hypotensive effect of *C. gileadensis* results from the activation of muscarinic cholinergic receptors in the brain (Abdul-Ghani and Amin, 1997) because the hypotensive effect was inhibited by pretreatment with atropine sulfate (1-4 mg/kg). In addition, the leaves and flowers of the plant were used by local Arab populations as analgesic, laxative and diuretic agents (Abdul-Ghani and Amin, 1997). Another study on rats using a verified plant extract showed a positive influence in the treatment of experimentally produced stomach ulcers. After 250 and 500 mg/kg balsam extracts were administered orally, the rats were protected against ethanol-induced depletion of stomach-wall mucus and a reduction in non-protein sulfhydryl (NP-SH) concentrations. Ethanol treatment also caused histopathological lesions of the stomach wall. Pre-treatment with balsam extract provided complete protection of gastric mucosa by supporting both the offensive and defensive factors (Al-Howiriny et al*.,* 2005).

MATERIALS AND METHODS

Apart from these reports, it is astounding that no serious investigation has ever been carried out on the composition of the liquid sap that is exuded from *C. gileadensis.* We report here, for the first time, an exami-nation of balsam in order to verify some of the medicinal properties recorded in the ancient literature. For this purpose, we conducted some preliminary experiments to determine the susceptibility of various bacteria to the sap and to look for the presence of infection-healing constituents in the plant.

Determination of the susceptibility of some pathogenic bacteria to *C. gileadensis sap*

The antimicrobial effect of *C. gileadensis*

In this study, we examined the efficiency of *C. gileadensis* saps as a treatment against a pathogenic clinical isolate of *E. coli* (strain kindly provided by Dr. Tzipora Lazarovitch, Head of the Clinical Microbiology Laboratory at Assaf Harofe Hospital, Israel) and an environmental isolate of *Bacillus cereus* (strain kindly provided by Prof. Yeshayahu Nitzan, Chief of the Medical Microbiology Laboratory at Bar-Ilan University, Israel).

The starter cultures of *E. coli and B. cereus* were grown aerobically overnight at 37°C on plates containing Brain Heart Infusion agar. Colonies were transferred to Brain-Heart Infusion broth to obtain an optical density of $A_{660} = 0.1$. The cultures were agitated at 180 rpm to obtain exponential growth ($A_{660} = 0.4$). The cells were then diluted at 1:100 and spread uniformly on agar plates containing the indicated medium. Bactericidal activity was determined using the Kirby-Bauer method (Bauer et al., 1966). Six-millimeter-diameter discs saturated with *C. gileadensis* saps were placed on the surface of the plates, which were then incubated aerobically for 24 h at 37°C.

C. gileadensis sap comes in two forms: one that is exuded immediately upon wounding is transparent and spreads quickly over the surrounding plant surface, and the subsequent one is milky and more viscous. We used two sets of six discs, one for the milky sap and the other for the transparent (serum-like) sap or other natural extracts. Since the saps were dissolved in ddH_2O, the control discs were also saturated with ddH_2O. The antibacterial activity of the plant saps and extracts was determined by measurement of inhibition-zone diameter (mm).

The experiment was repeated in triplicates and the mean values were recorded. Brain heart (BH) medium is known to contain a high level of protein, 15 times more than in Nutrient Broth (NB) medium (Nitzan et al., 1998). In order to see whether bacterial growth inhibition is medium-dependent, parallel experiments were carried out with nutrient agar (NA) medium.

We examined both types (serum and milky sap) of *C. gileadensis* as well as the sap of *Liquidambar orientalis*. The results showed that the thick milky, viscous *C. gileadensis* sap significantly inhibited *B. cereus* growth, exhibiting a zone inhibition diameter of 12 mm, while neither the thin, transparent, less-viscous sap nor the *Liquidambar orientalis* sap exhibited any activity against these bacteria. In addition, *E. coli* was not affected by the different saps. Moreover, it seems that *B. cereus* growth inhibition was not medium-dependent because there was no significant difference between inhibition zones on brain heart agar (BHA) compared to those on NA.

RESULTS

Effect of balsam sap on *Pseudomonas aeruginosa* lectin-dependent adhesion to target cells

Pseudomonas aeruginosa is an opportunistic human pathogen that can infect nearly any tissue or organ in the human body, including eyes, skin, ears, nose, throat, lungs, heart, kidneys, urinary tract, digestive system, liver, spleen, bones, and the meninges (membranes enveloping the brain and spinal cord). This bacterium is a most common cause of burn and ear infections and may infect the lungs of cystic fibrosis patients. It can contribute to blood poisoning and result in death (Gilboa-Garber, 1996; Gilboa-Garber et al., 1994, 1997).

The adhesion of this bacterium to human and other animal cells involves diverse adhesins, including two lectins PA-IL which binds D-galactose, and PA-IIL, which binds Lfucose (Gilboa-Garber, 1982 These lectins are important for the function and survival of *P. aeruginosa*.

They mediate the binding of the rod-shaped bacteria to one another (biofilm production), to other cells, to macro-molecules, and they also serve to protect the microorganism against antibodies and phagocytes. Their levels increase under stress situations in nature or in the host body due to the stimulation of their production by "quorum-sensing" signals (autoinducers and related factors) (Gilboa-Garber, 1997). The lectins' contribution to infection is associated with their specific saccharide-binding function, mediating specific adhesion of the bacterium to glycosylated compounds on host target cells. This adhesion may be abrogated by sugars which bind to the lectins as decoys and competitively block their adhesion to the target cells (Gilboa-Garber, 1997). Human milk and royal jelly, which protect neonates against infections, are rich in sugar-bearing compounds that block the *Pseudomonas aeruginosa* lectins (Lesman-Movshovich and Gilboa-Garber, 2003; Lesman-Movshovich et al., 2003; Lerrer et al., 2007).

Based on many historic reports on the healing properties of balsam products, we looked for the presence of lectin-binding sugars that function as decoys in *C. gileadensis* sap, proposing that such glycosylated substances might contribute to the therapeutic properties of the sap by binding to the bacterial lectins and blocking their attachment to the host cells. Clinical trials showed the efficiency of honey in the treatment of *P. aeruginosa* skin infections (Cooper et al., 2002). The balsam was found to block the *P. aeruginosa* lectin hemaggluinating activity using hemagglutination inhibition test, as was shown with human milk (Lesman-Movshovich and Gilboa-Garber, 2003; Lesman-Movshovich et al., 2003), royal jelly, and honey (Lerrer et al., 2007).

PA-IL (which is specific for D-galactose and its derivatives) and PA-IIL (which displays a very high affinity to L-fucose, but also recognizes that arabinose, mannose, and fructose) were prepared from *P. aeruginosa* ATCC 33347 (Gilboa-Garber, 1982). Since the sap of *C. gileadensis* has properties that would interfere with bacterial lectin-dependent adhesion, these preliminary findings are in agreement with the old claims praising balsam's medicinal qualities. They correlate the recent observations regarding myrrh and frankincense trees, which are species of the same family as balsam (*Burseraceae*). The latter has been studied in detail and found to contain materials of great medicinal value, which have been isolated. These components include antiseptic substances, resins that act as preservatives and anti-oxidants, insect repellents, as well as many other useful compounds (Assimopoulou et al., 2005; Hanuša et al., 2005).

Conclusions

The preliminary studies described in this work have shown that *C. gileadensis* possesses antibacterial activities that validate its usage in the local treatment of wound infections. Further research using additional pathogenic microbes and *in-vivo* experiments in animals is required in order to expand these findings.

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