



Traditional wound-healing plants used in the Balkan region (Southeast Europe)



Snežana Jarić*, Olga Kostić, Zorana Mataruga, Dragana Pavlović, Marija Pavlović, Miroslava Mitrović, Pavle Pavlović

Department of Ecology, Institute for Biological Research 'Siniša Stanković', University of Belgrade, Bulevar Despota Stefana 142, 11060 Belgrade, Serbia

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ABSTRACT

Ethnopharmacological relevance: The geographical and ecological specificity of the Balkan Peninsula has resulted in the development of a distinct diversity of medicinal plants. In the traditional culture of the Balkan peoples, plants have medicinal, economic and anthropological/cultural importance, which is reflected in the sound knowledge of their diversity and use. This study analyses the traditional use of medicinal plants in the treatment of wounds and the pharmacological characteristics of the most frequently used species.

Materials and methods: A detailed analysis of the literature related to ethnobotanical uses of medicinal plants in the Balkan region was carried out. Twenty-five studies were analysed and those plants used for the treatment of wounds were singled out.

Result: An ethnobotanical analysis showed that 128 plant species (105 wild, 22 cultivated and 1 wild/cultivated) are used in the treatment of wounds. Their application is external, in the form of infusions, decoctions, tinctures, syrups, oils, ointments, and balms, or direct to the skin. Among those plants recorded, the most commonly used are *Plantago major*, *Hypericum perforatum*, *Plantago lanceolata*, *Achillea millefolium*, *Calendula officinalis*, *Sambucus nigra*, *Tussilago farfara* and *Prunus domestica*. The study showed that the traditional use of plants in wound healing is confirmed by *in vitro* and/or *in vivo* studies for *P. major* and *P. lanceolata* (3 laboratory studies for *P. major* and 2 for *P. lanceolata*), *H. perforatum* (5 laboratory studies and 3 clinical trials), *A. millefolium* (3 laboratory studies and one clinical trial), *C. officinalis* (6 laboratory studies and 1 clinical trial), *S. nigra* (3 laboratory studies) and *T. farfara* (one laboratory study).

Conclusion: The beneficial effects of using medicinal plants from the Balkan region to heal wounds according to traditional practices have been proven in many scientific studies. However, information on the quantitative benefits to human health of using herbal medicines to heal wounds is still scarce or fragmented, hindering a proper evaluation. Therefore, further studies should be aimed at isolating and identifying specific active substances from plant extracts, which could also reveal compounds with more valuable therapeutic properties. Furthermore, additional reliable clinical trials are needed to confirm those experiences encountered when using traditional medicines. A combination of traditional and modern knowledge could result in new wound-healing drugs with a significant reduction in unwanted side effects.

1. Introduction

The existence of traditional medicine depends fundamentally on plant species diversity and the related knowledge of their use as herbal drugs. Out of an estimated 250,000 flowering plant species globally, between 50,000 and 70,000 are known to be used in traditional and modern medicine across the world (Leaman, 2006). Of all the plant species worldwide, 15% have been evaluated phytochemically and only 6% have been screened for biological activity (Verpoorte, 2000). In the Balkan region, no data is available on the total number of medicinal

plant species; however, there is data for particular countries: Serbian ethnomedicine today has knowledge of approximately 700 species, 420 of which are officially registered, and about 270 are available to buy (Kišgeci and Sekulović, 2000); in Bulgarian flora there are 768 medicinal plants and 764 are of indigenous or adventive origin (Gussev, 2005); in Romania, out of more than 3600 species of higher plants, over 700 are medicinal plants (Parvu, 2002; Tudor and Minoiu, 2004); in Montenegro there are around 700 medicinal plants, approximately 300 of which are used in traditional medicine as well as in the pharmaceutical industry (Pulević, 1965; Pulević, 1980); in Bosnia and

* Corresponding author.

E-mail address: nena2000@ibiss.bg.ac.rs (S. Jarić).

Herzegovina there are 221 medicinal plants used for ethnopharmacological purposes (Redžić et al., 2007). For other countries in the region no complete data is available. Medicinal plants are important sources of chemical substances that have beneficial therapeutic effects on human health, and plant-based systems continue to play an essential role in the primary healthcare of almost 65% of the world's population (Farnsworth et al., 1985) and 80% of the people in the world's underdeveloped and developing countries (Maver et al., 2015). In less wealthy rural areas or during times of economic crises, medicinal plants are relied upon as home remedies for health problems (Leonti, 2011).

The ethnomedicinal use of plants in the treatment of wounds (in the form of teas, decoctions, tinctures, syrups, oils, ointments, poultices, and infusions) is not only cheap and accessible, but provides a reliable natural resource of medicinal substances. Studies on medicinal plants have confirmed that herbal drugs exhibit fewer side effects in comparison to chemical agents, and are more cost-effective (Kumar et al., 2007; Rhoads et al., 2012). As medicinal plants provide this important resource of substances with beneficial therapeutic effects, they have been the subject of extensive research in the area of wound healing management (Nagori and Solanki, 2011; Kumar et al., 2013). Just 1–3% of chemicals listed in Western pharmacopoeia are indicated for the treatment of wounds and skin disease, while more than 30% of herbal medicaments are considered beneficial (Kumar et al., 2007; Rhoads et al., 2012). In recent times, pharmacological reports justify the traditional use of certain species of medicinal plants in the treatment of wounds (Gupta and Jain, 2010; Nagori and Solanki, 2011; Raina et al., 2008; Ajose, 2007). Many phytopharmaceutical laboratories are now concentrating their efforts on identifying the active constituents and models of action of various medicinal plants (Hwang et al., 2000) and a number of herbal products are being investigated at present to this effect, too.

While current therapeutic agents have generally inadequate efficacy and a number of serious adverse effects, medicinal plants have been used in medicine since ancient times and are well known for their ability to promote wound healing and prevent infection without any grave side effects. Thus, herbal therapy may be an alternative strategy for the treatment of numerous health issues including wounds (Budovsky et al., 2015). Therefore, more recently scientists have been increasingly relying on modern scientific methods and evidence-based medicine to prove the efficacy of herbal medicines and focusing on a better understanding of the mechanisms of their actions. However, information concerning the quantitative human health benefits of herbal medicines is still rare or fragmented, hindering a proper evaluation.

In this regard, this study provides an overview of ethnobotanical research into the use of wild and cultivated medicinal plants in the treatment of wounds in rural areas of the Balkan Peninsula. The plant parts used, as well as their preparation and administration, are noted. Special attention is given to the most commonly used species and the key laboratory experiments as well as clinical trials proving the efficacy of using herbal medicines in the healing of wounds.

2. The Balkan Peninsula as a centre of diversity of medicinal plants

The Balkan Peninsula (the Balkans) lies in the south-eastern part of Europe between 35°46'53"N and 13°23'30"E and is surrounded by the Adriatic, Ionian, Aegean, Marmara and Black Seas. Its area is approximately 505,578 km² and geopolitically it comprises the countries: Albania, Bosnia and Herzegovina, Bulgaria, Macedonia, Montenegro, Greece, Serbia, the European part of Turkey, Croatia, Slovenia and Romania (Fig. 1).

It is inhabited by around 50 million people (Grčić et al., 2013). Historically, it represents the crossroads between ancient European and Asian cultures, which has resulted in the presence of different ethnic and religious communities. Due to political turmoil in the past, many areas of the Balkan Peninsula have been subjected to political and

economic changes that have heavily influenced local lifestyles, economies, food, connection to nature, and consequently, the passing on of traditional knowledge of health and local complementary and alternative medical practices.

The Balkan Peninsula is one of 25 'hot spots' of plant biodiversity and is home to between 7000 and 8000 species of vascular plants (Stevanović et al., 1995), around 30% of which are endemic. The extraordinary diversity and endemism of the flora has mostly been shaped by the age of the Balkan landmass and its specific geographical position, as well as the diversity of climatic influences, geological composition, and orographic factors, which brought about the genetic isolation of populations and prompted their speciation. The existing ecological distinctiveness of the different parts of the Balkans has resulted in the development of specific genetic potential in certain plant species to produce active ingredients, making the area a centre of diversity of medicinal flora found in different ecosystems and on different geological substrates and soils.

Phytogeographical and ecological characteristics, as well as the demographic and ethnic structure of the Balkans, certainly had a role in the development and knowledge of ethnobotany and ethnomedicine, especially in rural areas. Traditional knowledge of plants for medicinal uses in rural areas has significant potential and demonstrates the links between plants and local people. With this in mind, ethnobotanical research into medicinal plants was carried out in some rural regions of the Balkans, with descriptions of their use and importance to the local population. There are many reasons for this type of study: 1) this mountainous region is a hotspot for both bio- and cultural/ethnic diversities; 2) historically, the area has provided botanical materials to the western European herbal market (especially in the last few centuries); 3) most dried medicinal plants and an impressive number of locally gathered plants are still widely used in local healthcare; 4) many economic initiatives and programmes devoted to rural development are based on medicinal plants (Quave et al., 2012).

For most of the peoples living in the Balkans, medicinal plants have therapeutic, commercial and anthropological cultural significance and are a symbol of good health. The reasons for the specific uses of plants for numerous health problems and diseases have gradually come to light over time, so their use has gradually emerged from an empirical framework to being based on explainable facts (Parojčić and Stupar, 2003; Jarić et al., 2014).

3. Background to wound healing

Wounds are any disruption to the normal anatomic structure of tissue which leads to the loss of epithelial continuity with or without a loss of underlying connective tissue, as well as the anatomic and functional integrity of the living tissue (Lazarus et al., 1994; Ramzi et al., 1994; Strodtbeck, 2001). There are various types of wounds, including incised wounds, lacerated wounds, abrasions, contusions, ulcers, and burn wounds (Leaper and Gottrup, 1998). Wound healing is a complex process which comprises three phases: inflammation, proliferation and maturation, and involves the well-organised and highly complex interaction of different tissues and cells with successive stages overlapping (Sidhu et al., 1999). The inflammatory phase starts as soon as injury occurs, with initial vasoconstriction allowing homeostasis and then inflammation mediators are released. Proliferation follows with the wound being rebuilt with new granulation tissue formed mostly by fibroblast and a new network of blood cells develop through the process of angiogenesis. Maturation involves remodelling and an improvement in collagen fibre components, leading to an increase in tensile strength (Mandelbaum et al., 2003). Parallel to this, scar formation occurs along with the accumulation of fibrous tissue at the edges of the wound, which eventually merges with surrounding tissue. However, there are numerous factors that lead to a delay in the healing of wounds, such as contaminated infective microorganisms, nutritional deficiency, interrupted blood supply and the improper movement of the disturbed body

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