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Herbal Remedies in Plant Management Their Evidences and Challenges with a Focus On "White Willow Bark"

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Abstract- ***Pain has been recognized as important in the primary care of patients with chronic conditions. Pain as a global public health priority, is an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage. Willow bark extract has been used for thousands of years as an anti-inflammatory, antipyretic, and analgesic also used as in pain management. Salix alba (SA), commonly known as white willow, is a plant used in folk medicine. The phytochemical characteristics of the bark extract of this plant indicated that its main component is salicin, which is precursor of the anti-inflammatory agent acetylsalicylic acid. White willow bark has the property of showing gram-negative intestinal bacteria. White willow bark medicinal plants genotoxic effect in human white blood cells. an observational study with a single extract of willow bark (Assalix®) under conditions of daily practice in Switzerland. . A small number of clinical studies have been conducted that support the use of willow bark extracts in chronic lower back and joint pain and osteoarthritis. Willow bark extracts also are widely used in sports performance and weight loss products doubtless because of anti-inflammatory and analgesic activities, although no human studies have been published that specifically and directly document beneficial effects. Various grades of the white willow bark extract are commercially available and contain, for example, 15%, 25%, or 50% salicin. Historically, willow bark has been used for over 2000 years.***

Index Terms- ***Salicin, Antipyretic, Genotoxic, Historically, Joint pain***

I. INTRODUCTION

In the primary care patients with long-term illness, pain has been recognized as an important factor. Although there is no much information on their effectiveness. Key component of overall health is oral health. Herbal remedies and other complementary and alternative therapies are not yet include in the main stream medical system. All age group are becoming more and more interest in herbal medicine, and the global market for it is expanding. In adult, pain is one of the most prevalent ailments for which herbal remedies are used. Herbal remedies, however, raise safety issues and may reduce the effectiveness of traditional treatments. In many ancient medical system, plant are always the main source of medication or treatment plan. The world health organization states that many populations use herbs or herbal products for basic medical requirements.

Herbal medicines are a method of treatment and prevention of a wide variety of diseases by using plant or plant products. Americans spend billions of dollars annually on complementary and alternative medicine, including herbal therapies. Willow bark extract has been used for thousands of years as an anti-inflammatory, antipyretic, and analgesic. Since ancient times preparations from *Salix* species have been used to alleviate pain. The aim of this study was to update the evidence of the effectiveness of willow bark products in the treatment of musculoskeletal pain. A small number of clinical studies have been conducted that support the use of willow bark extracts in chronic lower back and joint pain and osteoarthritis. Willow bark extracts also are widely used in sports performance and weight loss products. One notable example of a plant with medicinal properties is white willow (*Salix alba* L.), a member of the genus *Salix* and the family *Salicaceae*. Willows are a diverse group of plants, ranging from small shrubs to towering trees, with white willow typically falling on the smaller end of the spectrum. White willow, also known as salicin willow, has a long history of use for its health benefits, spa*nn*ing thousands of years.

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Arthritis is a chronic inflammatory condition that affects millions of individuals worldwide. Osteoarthritis (OA) is a joint disease involving not only articular cartilage but also the synovial membrane, sub-chondral bone and per articular soft tissues. *White willow bark* commonly known as white willow, is a plant used in folk medicine for the treatment of chronic and acute inflammation, infection, pain, and fever. Everyone can related to the concept of pain is part of everyday life. Ancient time's preparations from *Salix* species have been used to alleviate pain. The aim of this study was to update the evidence of the effectiveness of willow bark products in the treatment of musculoskeletal pain. OVID (MEDLINE), PUBMED, Silver platter, and CENTRAL and manual searches were used to identify clinical trials investigating *Salix* preparations. White willow contains a substance salicine that is converted by the body into a salicylate similar to the blood-thinner aspirin. Over the last twenty years, yet another use for aspirin has emerged connected with the discovery of its anti-thrombotic action. Arthritis is a joint disorder featuring inflammation. A joint is a part of the body where two dissimilar joints meet. A joint role to change the body portions associated by its bones. Various pharmacological mediators can stop or relieve the short-term pain and reverse the progression of physical damage. A number of anti-inflammatory drugs used in the treatment of arthritis have been developed over the past few decades, but there is still an urgent need for more effective drugs with lower side effects.

North American used the Bark or leaves to relive pain, inflammation and fever. The inner bark of white willow contain phenolic glycoside ester. American folk medicine also utilized a blood thinner and treat pain. White willow bark family includes a considerable number of species only the few are widely recognized as sources of medicinal bark: the European white willow (*salix alba* ; used since the beginnings of recorded histoty) , crack willow (*salix fragilis*), violet willow (*salix daphnoides*) and black willow (*salix nigra* ; most widely used by native Americans) Willow bark was included as part of the *Materia Medica* in the first volume of the U.S. Pharmacopeia published in 1820. Today, willow bark is used for the treatment of pain, particularly, LBP, osteoarthritis (OA), headaches, and inflammatory conditions such as tendinitis and bursitis. In the U.S., willow bark is a dietary ingredient in numerous DSs available in the market. Because of its popularity, the United States Pharmacopoeia (USP) developed quality standards for willow bark ingredients under the title *Salix* Species Bark. Prior to developing a DS monograph, USP customarily performs an Admission Evaluation. The chronological history of the discovery of willow as a medicinal plant can be sorted into three stages: the clinical potential of willow, structural elucidation of the phytotherapeutic salicin, and the chemical synthesis of salicylic acid and aspirin.

II. MATERIAL AND METHODS

One of the first natural analgesics is the bark of the *salix alba* (white willow). It contains salicin, a substance that functions in the human body very similarly to aspirin. In order to determine how effective it is in managing pain, it is typically necessary to gather the bark, make an extract from it, identify the compounds it contains, and then use safe, conventional scientific testing to determine how effectively it relieves pain in animals.

a) Plant matter:

The primary component is the white willow tree's (Salix alba) bark.

You can buy the bark from herbal store or gather it straight from the tree.

It is essential that the plant is correctly identified by a botanist.

After collection, the bark is cleaned to remove dirt or dust, then dried in the shade (not in direct sunlight) to protect its active ingredients.

Once dry, the bark is crushed into small pieces and ground into a fine powder.
The powder is stored in airtight glass containers to prevent moisture, which could spoil it.

b) Chemicals and reagent:
To extract and test the compounds in the bark, researchers use some common lab chemicals:
Ethanol or methanol (for extraction of plant compounds).
Distilled water (for making solution).
Ferric chloride, hydrochloric acid, sodium hydroxide (for testing chemical compound).
Aspirin or ibuprofen (used as a standard drug to compare with the herbal extract).

c) Laboratory equipment:
The main instrument and tools needed include:
soxhlet extractor: -
Used to separate useful compounds from the powdered bark using solvents like ethanol.
Rotary evaporator: -
Used to remove the solvent gently and get concentrated extract.
Hot plate and water bath: -
For heating during extraction and drying.
Glassware: - this includes beaker, flasks, test tubes, and filter paper.

d) Experimental animals:
Small laboratory animals such as wistar rats or swiss albino mice are used to test pain relief.
The animals are kept in clean cages under proper light and temperature conditions.
They are given a normal diet and water and allowed to adjust to the environment before experiments starts.
All experiments are carried out ethically, with prior approval from the institutional Animal Ethics Committee (IAEC)

Methods:
a) Making the extract
1. Weighing the powder: A predetermined quantity of dried, powdered bark is taken, such as 250 grams.
2. Extraction: ethanol is used as the solvent and the powder is put inside a Soxhlet extractor. The active ingredients, such as salicin and flavonoids, are extracted from the bark powder by continuously passing the solvent through it. Typically, this process takes six to eight hours to complete.
3. Filtration: To get rid of solid particles, the mixture is filtered after extraction.
4. Concentration: The solvent is slowly removed from the liquid extract by heating it in a rotating evaporator.
5. Drying: To create a solid or semi-solid bulk, the leftover viscous extract is further dried.

b) Phytochemical screening:
Flavonoid test: add magnesium and hydrochloric acid results in a red or pink color means flavonoids are present.
Tannins test: add few drop of ferric chloride results in a dark blue or green color means tannins are present.
Phenolic compound: show a blue – black color with ferric chloride.

Phytochemistry
The genus Salix, which includes willow trees, contains secondary metabolites or phytoconstituents. A varied class of secondary metabolites found in plants, flavonoids are well-known for their numerous health advantages and antioxidant qualities. Fruits, vegetables, and drinks like tea and wine frequently contain them. A sugar molecule joined to a non-sugar component is known as a glycoside. They can be further divided into non-phenolic glycosides and phenolic glycosides, which are glycosides with a phenolic group. Procyanidins, sometimes referred to as condensed tannins, are oligomeric flavonoids. They are recognized for their antioxidant qualities and can be found in a variety of plants. Plants frequently contain organic acids including citric, malic, and tartaric acids.

Esters, salts, and other substances made from organic acids are examples of their derivatives. The presence of a phenol group is what distinguishes phenolic substances.

Among their many functions in plants is protection against environmental stresses and infections. One class of lipid that contributes to the structural integrity of cell membranes is sterol. Terpenes are a broad family of chemicals with a variety of biological functions that are produced from isoprene molecules.

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Plants contain phenolic chemicals called lignans, especially in their cell walls. They have estrogenic and antioxidant qualities. Organic molecules with low molecular weights that readily evaporate at room temperature are known as volatile chemicals. Long-chain carboxylic acids, or fatty acids, are frequently present in fats and oils.

Phenolic Glycosides

The distribution and classification of phenolic glycosides within the Salicaceae family, with a special emphasis on the species Salix, are significant. As secondary metabolites, these glycosides are significant and can be used as taxonomic markers for various Salix species. Different Salix species can be distinguished from one another by the presence of certain glycosides such as salicin, tremuloidin, and tremulacin, as well as others like acmophyllin A and B, chaenomeloidin, cochinchiside, lasiandrin, leonuriside, and salicin-7-sulfate. Additionally, the discovery of specific glycosides, including acutifoliside and 1,2-cyclohexanediol glycosides, helps to characterize and classify Salix plants by acting as chemical markers for particular plant sections, such as juvenile stems or twigs. All things considered, the distribution and existence of these phenolic glycosides offer important information about the phytochemistry and taxonomy of Salix species.

Pharmacological Activity

Are well know the traditional use of various *Salix* species and their isolated com-pounds, such as salicylic acid and salicin, in folk medicine to treat various ailments in-cluding rheumatic diseases, back pain, toothache, headache, and menstrual cramps. Additionally, it mentions the diverse range of biological activities exhibited by *Salix* species and their compounds, including analgesic, anti-inflammatory, antioxidant, anticancer, cytotoxic, antidiabetic, antimicrobial, anti-obesity, neuroprotective, and hepatoprotective activities.

Specifically, salicylic acid is noted for its effects on cyclooxygenases (COX I, II), which are enzymes crucial for the synthesis of prostaglandins, molecules involved in inflammation and pain regulation.

Anti-inflammatory Activity Inflammation and its consequences: Inflammation is a common response to various stimuli such as microbial infection and injury. While inflammation is essential for controlling infection and promoting tissue repair, unresolved inflammation can contribute to the pathogenesis of diseases like atherosclerosis, obesity, cancer, and inflammatory bowel disease.

III. METHODS

HPLC Method

Salicin, found in willow bark, has garnered attention for its therapeutic properties, particularly its anti-inflammatory effects. Single drug therapy is focusing on the use of a single medication for treating a particular condition, has a long history dating back to ancient times [44,45]. It's widely accepted by physicians today for various diseases. With the increased use of herbal remedies alongside conventional medications, understanding interactions between herbs and drugs has become crucial in clinical practice to ensure safety and efficacy. Developing a marker profile is vital for quality control and scientific validation of single drugs. This ensures consistency in composition and potency, aiding in reliable therapeutic outcomes. It’s described as the metabolic precursor.

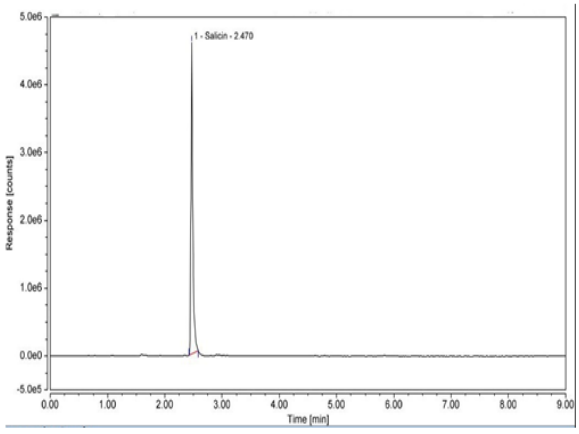

Figure: Concentration of Salicin from *Salix alba* bark

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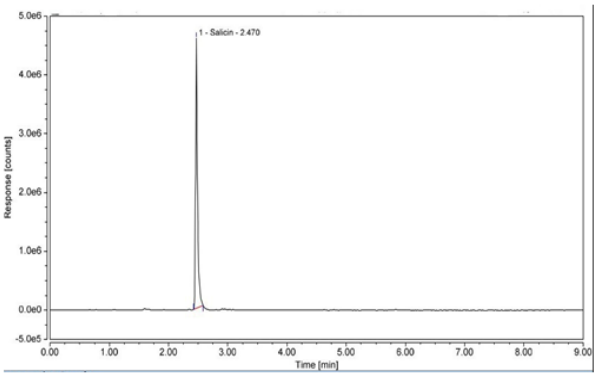

figure: Concentration of Salicin from *Salix babylonica* bark

of salicylic acid, possessing anti-inflammatory properties. Salicin is an alcoholic beta-glycoside containing D-glucose, found in willow barks, particularly in *Salix alba L* (White Willow). It's noted as a weaker forerunner of aspirin. Willow bark contains various chemical compounds, including glycosides (such as salicin), tannins, aromatic aldehydes and acids, salicyl alcohol (saligenin), and flavonoids. These constituents contribute to its pharmacological effects. Salicin exhibits antipyretic and analgesic effects, making it useful in treating fever and conditions like arthritis. Its similarity to aspirin in action.

HPLC was performed using an Agilent EZChrom Elite system equipped with a DAD detector and a HiCHROM LiChrosorb 100 RP-18 column, 10 µm particle (4.6 x 250 mm).Extraction of salicylic derivatives: for the analysis of the samples represented by branches of willow. The sample (1 g) was extracted with 8 mL of a solution consisting of a part of 4.2 g/L NaOH solution and a part of methanol. The mixture was stirred at 60°C at reflux for 60 min. After cooling, 0.4 mL of 10 g/L HCl solution was added and the mixture was centrifuged at 9000 rpm for 5 minutes. The supernatant was diluted to 10 mL with a mixture of equal volumes of methanol and high purity water. Before HPLC analysis, the samples were filtered with a PA filters.
Salicin derivatives are the main constituents of willow bark and can be quantified as salicin equivalents. According to the Monograph of the European Pharmacopoeia and the Evaluation Report of the European Medicines Agency, the content of salicin derivatives in the bark of different species of willow varies from 0.5 to 10%. However, quality standards involve at least 1.5%.Although willow bark remains the main source of salicin.

Extraction method for an aqueous extracts
We prepare the aqueous extracts from *Salix alba* bark

Preparation of stock aqueous extracts: 10 grams of air-dried and milled plant material are soaked in 100 ml of distilled water, resulting in a concentration of 10% (w/v).The soaking occurs at room temperature (°C) for 24 hours with occasional shaking to facilitate the extraction process.

Filtration and centrifugation: after 24 hours of soaking, the mixtures are filtered through two layers of cheesecloth to remove solid particulate materials. The filtered mixtures are then centrifuged for 20 minutes at 10,000 rpm. This step helps to further remove any remaining particulate matter and debris, resulting in purified extracts.

Adjustment of pH: the purified extracts are adjusted to a pH of 6.8 using 1.0 M HCl (hydrochloric acid). pH adjustment is often done to optimize the stability and solubility of bioactive compounds present in the extract.

Storage: finally, the adjusted extracts are stored in the refrigerator at 4°C for future use. Storing the extracts at low temperature helps to preserve the stability and integrity of the bioactive compounds present in the extract. This method ensures the extraction of water-soluble compounds from the plant material and results in purified aqueous extracts suitable for further analysis or use in various applications such as pharmaceuticals, cosmetics, or food products.

IV. RESULT

The review of clinical studies reveals that white willow bark (*salix alba*) exhibits promoting analgesic (pain relieving) and anti-inflammatory properties. Its therapeutic benefits are mainly attributed to active compound salicin, which is converted in the body to salicylic acid. A natural precursor to moderate aspirin. In addition to salicin, other phytochemicals

such as flavonoids, polyphenols, and tannins contributes synergistically to its overall pharmacological effects.

V. CONCLUSIONS

The review concludes that white willow bark is one of the most scientifically supported herbal remedies for pain management, particularly in conditions such as osteoarthritis, lower back pain and musculoskeletal inflammation. Its main bioactive constituents, salicin, along with other phenolic compounds, flavonoids, and tannins, contributes to significant analgesic and anti-inflammatory effects that resemble those of aspirin, but with fewer gastrointestinal and systemic side effects. Evidence from multiple clinical trials, and pharmacological studies supports the traditional use of white willow bark in reducing pain intensity and improving functional outcomes. the potential clinical benefits of willow bark for pain relief and the improvement of physical function in patients with arthritis. In addition, there were no significant differences in the risk of adverse events among patients with arthritis between the willow bark and analgesics or placebo groups. These adverse events mainly consisted of skin and appendage disorders, gastrointestinal system disorders, and infections associated with using willow bark.

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