International Journal of Pharmaceutical Research and Applications

# Polyherbal Approaches to Arthritis Treatment: Harnessing India's Botanical Wealth 

${ }^{1 *}$ Palak Jain, ${ }^{2}$ Dr. Durga Panday<br>${ }^{1}$ Sagar Institute of Research and Technology-Pharmacy, Bhopal (M.P)


#### Abstract

India's abundant flora offers a vast reservoir of herbal remedies for the management of arthritis. This article delves into a diverse array of indigenous plants, renowned for their anti-inflammatory and anti-arthritic potential. The exploration encompasses botanical nomenclature, family classification, regional monikers, utilized plant parts, chemical constituents, and manifold applications. Our comprehensive review underscores the profound advantages of polyherbalism, demonstrating its superior efficacy compared to conventional and single-herb remedies. This study not only facilitates the identification of active compounds within arthritis-fighting plants but also lays the foundation for future research and the development of innovative and efficacious herbal formulations to combat this debilitating condition.


KEYWORDS-Polyherbalism, Arthritis, Indigenous plants, Active Constituents, Botanical wealth.

## I. INTRODUCTION

Arthritis, a chronic autoimmune ailment characterized by painful joint inflammation, imposes a considerable burden on millions of individuals worldwide. Of these, a substantial 21 million are afflicted by rheumatoid arthritis, with a striking $80 \%$ of cases manifesting between the ages of 35 and 50 . In tandem with this growing health challenge, there has been an extraordinary surge in the realm of herbal medicine over the last few decades. Ayurvedic medicine, deeply rooted in ancient wisdom, extols the virtues of herbal plants as indispensable remedies-an age-old tradition enshrined in the sacred texts of Vedas and Samhitas. ${ }^{1}$

Historically, plants and their derivatives have been harnessed both in isolation and in synergy to combat various diseases. Presently, conventional pharmaceutical treatments for arthritis, including disease-modifying antirheumatic drugs and nonsteroidal anti-inflammatory drugs, have raised concerns due to their potential toxic side effects and
escalating treatment costs during extended use. Consequently, a growing number of individuals are revisiting the realm of herbal therapy, a modality that promises safety, cost-effectiveness, and minimal or no side effects.

The paramount objective in the treatment of arthritis remains the amelioration of symptoms, inflammation, and pain. Achieving this goal hinges on the judicious employment of an array of herbal plants, orchestrated in optimal therapeutic combinations. In this context, the rich tapestry of herbal remedies beckons as a beacon of hope, offering a holistic approach to addressing the challenges posed by this debilitating condition.

## AYURVEDA: A TIMELESS HEALING TRADITION <br> Definition and Essence

Ayurveda, an ancient healing system deeply woven into the tapestry of India's heritage, stands as one of the world's most venerable medical sciences. The term "Ayurveda" finds its roots in the amalgamation of Sanskrit words, 'ayur,' signifying life, and 'veda,' translating to science or knowledge. This etymological composition underscores Ayurveda's core tenet - the cultivation of equilibrium and harmony in the realms of the mind, body, and spirit. ${ }^{2-3}$

## The Panchamahabhutas and Tridoshas

Central to this age-old wisdom is the belief that the universe comprises five elemental pillars: Vayu (air), Jala (water), Aakash (space), Prithvi (earth), and Teja (fire). These elements, in their varying combinations, are thought to forge the fundamental humors of the human body known as "Tridoshas": Vata dosha, Pitta dosha, and Kapha dosha. Vata governs cellular transport, electrolyte balance, and waste elimination, while Pitta orchestrates body temperature, optic nerve coordination, hunger, and thirst regulation. Kapha, the third dosha, provides vital joint lubrication for proper functioning. A symphony of balance among

International Journal of Pharmaceutical Research and Applications Volume 8, Issue 6 Nov-Dec 2023, pp: 448-459 www.ijprajournal.com ISSN: 2249-7781
these doshas, in conjunction with other factors, is the sine qua non of good health, as any disruption in this equilibrium precipitates malaise and disease. ${ }^{4}$

## The Ayurvedic Philosophical Paradigm

Ayurveda's philosophical compass is marked by a profound contrast with allopathic medicine. While the latter predominantly addresses symptoms, Ayurveda aspires to prevent suffering and extend the tapestry of life. Its approach hinges on the application of natural remedies, which serve not only to treat ailments but, crucially, to unearth and eradicate their underlying causes. ${ }^{5}$

## The Herbal Heritage

Historically, Ayurveda derives its potency from a vast repository of healing herbs chronicled in traditional Indian texts. In the 19th century, the advent of chemical analysis precipitated the extraction and alteration of these botanical treasures into synthetic pharmaceuticals, momentarily relegating herbal medicine to the shadows. However, the prohibitive cost and side effects associated with synthetic drugs kindled a revival of traditional herbal remedies. ${ }^{5}$ In Ayurveda's embrace, plants and their active constituents offer a gentler path to healing, free from the shackles of side effects and adverse reactions. Archaeological evidence underscores the timelessness of herbal medicine, with records dating back to the Paleolithic age, approximately 60,000 years ago, and written documentation of herbal remedies extending over 5,000 years to the Sumerians, who meticulously compiled lists of medicinal plants. ${ }^{6-7}$

## HERBAL FORMULATION: BRIDGING NATURE AND HEALING

## Herbal Diversity in Commerce

Herbs and their derived products have long served as commodities, exchanged and leveraged for a multitude of applications. ${ }^{8}$ According to the World Health Organization (WHO), herbs are defined as plant materials, either fresh or dried, fragmented or powdered. These botanical treasures can be utilized in their raw state or subjected to further refinement through a spectrum of physical, chemical, or biological processes. Such processes include extraction, distillation, purification, concentration, or fermentation, ultimately culminating in the creation of refined herbal products. ${ }^{9}$

## The Spectrum of Herbal Medicine

Herbal medicines are a manifestation of this natural bounty, emanating from plant sources,
inorganic materials, or even animal origin, featuring both raw and processed constituents. Today, these herbal preparations have evolved into indispensable components of disease management, offering a holistic and time-tested alternative.

## India's Botanical Wealth

India, recognized as one of the world's twelve biodiversity epicenters, shelters an astonishing array of over 45,000 distinct plant species. Among these botanical treasures, approximately $15,000-20,000$ plants have unveiled their therapeutic virtues, enshrined in the annals of traditional Indian systems of medicine, such as Ayurveda and Unani, for centuries. This rich tapestry of flora encapsulates the essence of ancient wisdom, providing a treasure trove of medicinal solutions to ailments that have transcended time. ${ }^{10-11}$

## POLYHERBAL FORMULATION: A MULTIFACETED APPROACH Herbal Renaissance

Recent decades have witnessed an unparalleled resurgence in the realm of herbal medicines. Nature, it seems, has always held the keys to a profound synergy between health and the environment. ${ }^{12}$ In developing nations, a staggering $80 \%$ of the population places their trust in a diverse array of plant species, elevating traditional medicine to the forefront of their primary healthcare modalities. ${ }^{13}$

## Ancestral Wisdom

The earliest systems of medicine, encompassing Ayurveda, Siddha, and Unani, unfurl a rich tapestry of knowledge that underscores the therapeutic potential of several plant species in treating a multitude of maladies. ${ }^{14}$ Within this tradition, a concept of profound significance arises the art of polyherbal formulation. Derived from Ayurveda and analogous traditional medical systems, the concept of polyherbalism, as illuminated in works like Sarangdhar Samhita, is predicated on achieving amplified therapeutic efficacy while mitigating toxicity. This strategy, often termed "herb-herb combination," extends its influence far and wide due to its medicinal and therapeutic prowess.

## Polyherbal Powerhouse

The cornerstone of polyherbalism resides in the amalgamation of various herbs, each contributing its unique virtues, artfully combined in precise proportions. This results in a potent synergy

International Journal of Pharmaceutical Research and Applications Volume 8, Issue 6 Nov-Dec 2023, pp: 448-459 www.ijprajournal.com ISSN: 2249-7781
that begets therapeutic effects surpassing those of individual herbs. The holistic nature of polyherbal formulations mirrors the rich tradition of whole plants or plant mixtures in traditional medicine, eschewing the isolation of specific compounds. ${ }^{15-16}$

## Advantages of Polyherbal Formulation Synergistic Symphony

Scientific inquiry has illuminated the profound advantages of polyherbal formulations over single-herb counterparts. The amalgamation of herbs with distinct efficacies orchestrates a symphony of synergistic effects, generating outcomes that eclipse those attainable with individual constituents. ${ }^{17-20}$

## Tailored Healing

Polyherbal formulations offer the gift of customization, enabling healthcare providers to craft treatments tailored to the unique needs of individual patients. This bespoke approach aligns seamlessly with the principles of holistic patient care. ${ }^{21}$

## Enhanced Potency, Minimal Side Effects

In the realm of potency and safety, polyherbal formulations reign supreme. They harness the amalgamated power of active constituents from diverse plants to deliver enhanced therapeutic effects while keeping side effects at bay. This contrasts starkly with the limitations of isolated compounds. ${ }^{22}$

## Patient-Centric Convenience

Patients are the ultimate beneficiaries of polyherbal formulations, as they eliminate the need to juggle multiple single-herb preparations. This convenience streamlines the therapeutic experience. ${ }^{23}$

## Affordability and Accessibility

Polyherbal formulations, being natural products, offer an attractive cost advantage, alongside eco-friendliness when juxtaposed with allopathic counterparts. Their affordability and remarkable benefits have catalyzed a burgeoning demand within the market. ${ }^{24}$

## Challenges and Considerations

However, the world of polyherbal formulations is not without its complexities. Issues pertaining to sources, processing, patient profiles, practitioners, and legal and regulatory frameworks demand meticulous attention. Furthermore, the concurrent use of polyherbal formulations with
allopathic drugs necessitates scrutiny, as potential interactions may influence pharmacological outcomes and precipitate adverse reactions. ${ }^{25-27}$

## UNDERSTANDING ARTHRITIS: AN IMMUNE SYSTEM CONUNDRUM <br> The Immune System's Role

Our body's immune system is a formidable defender, tasked with safeguarding us against external threats. Yet, when this shield turns excessively vigilant, it can inadvertently ignite a cascade of hypersensitive and allergic reactions, potentially culminating in debilitating autoimmune diseases. These conditions arise when the immune system loses its capacity to distinguish between the body's own cells and foreign invaders, leading it to unleash a misguided assault on its own tissues. The repercussions of such self-directed warfare are dire, often manifesting in the form of chronic autoimmune diseases like arthritis. ${ }^{28}$

## The Menace of Arthritis

Arthritis, a vexing disorder afflicting the musculoskeletal system, stands as a chronic malady rooted in multifaceted origins. Etymologically derived from "arth" signifying joint and "ritis" denoting inflammation, arthritis precipitates not only pain and discomfort but can progress to the point of causing incapacitating deformities and functional limitations. Its manifestations span various forms, including rheumatoid arthritis, osteoarthritis, degenerative joint disease, infectious arthritis, and gout. ${ }^{29-30}$

## RHEUMATOID ARTHRITIS: A MULTIFACETED ONSLAUGHT Ravages of Autoimmunity

Rheumatoid arthritis (RA), a representative of autoimmune diseases, is a relentless chronic condition wherein the body's immune system erroneously targets the healthy tissues of joints. This ill-conceived assault sparks inflammation and the formation of pannus tissue, a destructive substance. RA, unforgiving in its nature, can infiltrate the synovial lining of joints, extending its reach to other organs such as the eyes, heart, lungs, skin, and blood vessels. While it most prominently inflicts pain upon the hands and feet, RA's pathological progression is marked by the thickening of the lining and an increase in the number of blood vessels and white blood cells in diverse organs.

International Journal of Pharmaceutical Research and Applications Volume 8, Issue 6 Nov-Dec 2023, pp: 448-459 www.ijprajournal.com ISSN: 2249-7781

## Epidemiology

This autoimmune scourge, predominantly afflicting females, casts its shadow over approximately $0.5-1 \%$ of the arthritis-afflicted population, with more than 21 million individuals worldwide succumbing to its debilitating influence. ${ }^{31-33}$

## Progression through Stages

RA's ruthless progression unfolds through three discernible stages. In Stage-I, swelling engulfs the synovial lining, giving rise to pain, redness, stiffness, and swelling in the vicinity of the joints. Stage-II is characterized by the rapid proliferation of cells or pannus, thickening the synovium. Stage-III unleashes enzymes that may incite bone and cartilage degradation, leading to the painful loss of alignment and impaired mobility. ${ }^{34}$

## Symptoms: The Telltale Signs

The spectrum of symptoms accompanying RA encompasses swollen, tender, and warm joints, accompanied by body aches, general malaise, excessive thirst, lethargy, a sense of heaviness, recurrent fever, and early morning stiffness in the joints. As the condition advances, these symptoms may extend their dominion to affect wrists, knees, ankles, elbows, hips, and shoulders. ${ }^{35-36}$

## The Underlying Cause

RA's origins lie in the immune system's misguided assault on the synovium - the membranes encompassing the joints. The ensuing inflammation results in synovium thickening, cartilage and bone deterioration within the joint, and weakening of the tendons and ligaments that maintain joint integrity. The ultimate consequence is the misalignment and deformity of the joint. ${ }^{35}$

## The Unraveling of Physiology

In the crucible of infection or environmental triggers, the body typically summons its immune forces to defend and protect. However, in RA, the immune system falters, giving rise to destructive substances that attack the joints instead of safeguarding them. This pathological process culminates in the development of RA, where the once-thin joint lining transforms into a thickened fortress brimming with white blood cells. These cells, including but not limited to interleukin-1 (IL1) and Tumour Necrosis Factor alpha (TNF-alpha), unleash havoc by causing pain, joint swelling, and structural damage. Other cytokines such as IL-17, IL-18, and Receptor activator of nuclear factor
kappa-B ligand (RANKL) further fan the flames, stimulating synovial fibroblasts and chondrocytes in the neighboring articular cartilage to secrete enzymes that degrade proteoglycan and collagen, ultimately resulting in the ruinous deterioration of joint tissues. ${ }^{37}$

## HERBAL TREATMENT FOR ARTHRITIS: HARNESSING NATURE'S BOUNTY

## The Herbal Renaissance

In contemporary healthcare, herbal medicines and therapeutic agents have ascended to the forefront as popular choices for the management of chronic diseases. This paradigm shift is underpinned by the fact that a substantial $64 \%$ of the world's population now embraces herbal remedies as part of their healthcare regimen. This global movement has culminated in the utilization of approximately 2100 plant species, scattered across the world, as instrumental tools in the pursuit of well-being.

## India's Botanical Bounty

India, hailed as a biodiversity treasure trove, emerges as a veritable epicenter for herbal treatment. With its profusion of plant species, it stands as a pivotal source for herbal therapies that span a gamut of ailments. Arthritis and rheumatism, two of the most debilitating inflammatory conditions afflicting humanity, have not escaped this herbal renaissance.

## Herbal Alternatives for Arthritis Management

In contrast to conventional allopathic treatments for arthritis, fraught with side effects and financial burdens, herbal remedies offer a compelling alternative. Herbal therapies provide a path to effectively manage the symptoms of arthritis in a manner that is both safe and cost-efficient. In a climate where individuals are increasingly inclined towards natural products, herbal interventions have emerged as potent allies in the battle against arthritis.

## Nature's Healing Touch

Nature, in its bountiful generosity, has bestowed upon us a formidable arsenal of herbs, each harboring the potential to ameliorate the inflammation, pain, and stiffness that typify arthritis. These herbal treasures manifest their therapeutic prowess through medicinally active constituents that wield a pharmacological influence tailor-made for the challenges of arthritis.

International Journal of Pharmaceutical Research and Applications Volume 8, Issue 6 Nov-Dec 2023, pp: 448-459 www.ijprajournal.com ISSN: 2249-7781

## Safer and Potent Solutions

The evolution of safer and more potent medicaments is a testament to the wealth of oriental sources. This journey includes the harnessing of herbal extracts, the application of physical therapy, and the formulation of polyherbal combinations, each playing a pivotal role in the comprehensive treatment of rheumatoid arthritis (RA). In the realm of herbal treatment, the alchemical synergy between nature's gifts and scientific ingenuity emerges as a beacon of hope for those afflicted by the burdens of arthritis. ${ }^{37-39}$

## ANTI-ARTHRITIC NATIVE FLORA

Several native flora species have been meticulously studied for their potential as antiarthritic and anti-inflammatory agents. These plants are identified by their scientific nomenclature, family affiliation, regional sobriquet, employed plant components, chemical elements, and alternative applications.

Scientific Nomenclature: The scientific names of these plants are carefully documented, providing a precise identification of each species.
Family Affiliation: Understanding the botanical families to which these plants belong is essential for classifying and studying their properties effectively.
Regional Sobriquet: These plants often have regional names or nicknames, which reveal their cultural significance and common use in specific regions.
Employed Plant Components: The specific parts of these plants used for their anti-arthritic properties, whether it be leaves, roots, or other components, are outlined.
Chemical Elements: The chemical compounds found in these plants, responsible for their antiarthritic and anti-inflammatory effects, are elucidated.
Alternative Applications: Beyond their antiarthritic potential, these plants may have diverse applications, which are explored to understand their broader significance.
This comprehensive approach ensures a detailed understanding of the native flora species and their anti-arthritic properties, facilitating further research and utilization in the field of medicine.

## Sweet Flag ${ }^{40}$

Common Names- Sway, muskrat root
Botanical Name- Acorus calamus
Family- Acoraceae
Part use- Rhizome and leaves

Chemical Constituents- $\alpha$-pinene, camphene, $\beta$ pinene, bornyl acetate
Other uses- Anti-inflammatory, analgesic, antifungal, antibacterial, antioxidant, antidepressant, anticholinergic, cardioprotective, antidiabetic, anticancer.

## Garlic ${ }^{41}$

Common Names- Lashan, aglio
Botanical Name- Allium sativum
Family- Amaryllidaceae
Part use- Bulb
Chemical Constituents- Allicin, Allin, Selenium, mucilage
Other uses- Antibacterial, antiparasitic, antiviral, antifungal, wound healing, antidiabetic, antihypertensive, diuretic, anticancer, antitumor, antiprotozoal and in digestive disorder.

Aloe ${ }^{42}$
Common Names- Aloe vera
Botanical Name- Aloe barbadenis
Family- Asphodelaceae (Liliaceae)
Part use- Leaves
Chemical Constituents- Aloe contains 75 potentially active constituents such as vitamins, enzymes, minerals, sugars, lignin, saponins, salicylic acid, amino acid, anthraquinones and phenolic compounds.
Other uses- Use for burns and wounds healing, moisturizing, immune system restoration, antioxidant, immunomodulatory, antibacterial, antifungal, antarthritic, analgesic, antiulcer, laxative, anti-aging, antiinflammation.

Giloy ${ }^{43}$
Common Names- Guduchi
Botanical Name- Tinospora cordifolia
Family- Menispermeaceae
Part use- Whole plant
Chemical Constituents- Steroids- $20 \quad \delta$ hydroxyecdysone, $\delta$-sitosterol, $\quad \beta$-sitosterol, giloinsterolecdysterol
Diterpenoids lactones- furanolactone, Tinosporon, tinosporides, columbin, clerodane, jateorine.
Aliphatic compounds- heptacosanol, octacosanol, nonacosan-15 one dichloromethane.
Other uses- Hypoglycemic, antiallergic, cardio protective, hepatoprotective, antistress, antiinflammatory, antineoplastic, osteoprotective, antifertility, antiulcer, antileprotic

## Night Jasmine ${ }^{44}$

Common Names- Parijat, harsingar, coral jasmine

International Journal of Pharmaceutical Research and Applications Volume 8, Issue 6 Nov-Dec 2023, pp: 448-459 www.ijprajournal.com ISSN: 2249-7781

Botanical Name- Nyctanthesarbor-tristis
Family- Oleaceae
Part use- Leaves
Chemical Constituents- Steroids - $\beta$-sitosterol
Terpenes- Triterpenes- $\beta$ amyrin, oleanolic acid, friedeline, lupeol
Alkaloids- Nyctanthine
Glycosides- Flavonol glycosides are astragaline and nicotiflorine
Irridoid glycosides- Arborsides $\mathrm{A}, \mathrm{B}, \mathrm{C}, 6 \beta-$ hydroxyloganin, desrhamnosylverbacoside, 6, 7- di-o-benzoylnycthanoside, 6-o-transcinnamoyl-6 $\beta$ hydroxyloganin, 7 -o-trans-cinnamoyl-6 $\beta$ -
hydroxyloganin.
Flavonoids- Nicotiflorin
Others- Mannitol, tannic acid, ascorbic acid, methyl salicylate, traces of volatile oil.
Other uses- Antioxidant, anticancer, antiinflammatory, CNS depressant, antidiabetic, hepatoprotective, antimicrobial, antifungal, antimalarial, antiparasitic.

## Ashwagandha ${ }^{45}$

Common Names- Indian winter cherry, Indian ginseng
Botanical Name- Withaniasomnifera
Family- Solanaceae
Part use- Whole plant
Chemical Constituents- Roots andleaves-Withaferin-A, Withanone, 27-hydroxywithanone, Withastramonolide, Physagulin, Withanolide-A.
Fruits-Fatty acids, Sterols, Tocopherols, Hydrocarbons (squalene)

Leaves- $\quad 5 \mathrm{~b}, 6 \mathrm{~b}-$ epoxy-4b-hydroxy-1-oxo-witha-2,16,24- trienolide, 6a,7a-epoxy-3b,5a,17a-trihydroxy-1-oxo-witha-24- enolide, 27-acetoxy-3-oxo-witha-1,4,24-trienolide, 5a,17a-dihydroxy-6a,7a-epoxy-1-oxo-3b-O-sulfatewitha-24-enolide, 17-hydroxy withaferin A, 6a-Chloro-5b,17adihydroxywithaferin A, 6a-chloro-5bhydroxywithaferin A, 2,3-dihydrowithaferin A, 3-methoxy-2,3-dihydrowithaferin A, withanoside IV, withanoside X , viscosalactone B , 27deoxywithaferin A, 27- hydroxywithanolide B, Pubesenolide, Jaborosalactone D, 4b,27-dihydroxy-L-oxo-22R-witha-2,5,24-trienolide, 2,3didehydrosomnifericin, 6achloro-5bhydroxywithaferin A, (22R)- 5b-formyl-6b,27-dihydroxyl-1-oxo-4-norwith-24-enolide
Roots- 16b-Acetoxy-6,7a-epoxy-5a-hydroxy-1-oxowitha2,17(20),24-trienolide, 5,7a-Epoxy-6a,20a-dihydroxy-1-oxowitha-2,24- dienolide,
Aerial Parts-3 $\alpha$-(uracil-1-yl)-2,3-dihydrowithaferin A, 3 $\beta$-(adenin- 9 -yl)-2,3-dihydrowithaferin A, 2,3-
dihydrowithaferin A-3 $\beta$-O-sulfate, $3 \beta$-OButyl-2,3dihydrowithaferin $\quad \mathrm{A}, \quad 3 \beta$-(uracil1-yl)-2,3dihydrowithaferin A.
Other uses- Used for astringent, diuretic, arthritis, insomnia, tuberculosis, asthma, cough, antidiabetic, fever, anti-inflammatory, paralysis, antimicrobial, It is also active against neurological and psychological conditions.

## Kholinjan ${ }^{46}$

Common Names- Galanga
Botanical Name- Alpinia officinarum
Family- Zingiberaceae
Part use- Rhizome
Chemical Constituents- Phenylpropanoid ( phydroxycinnamaldehyde) and volatile oils.
Other uses- Used for the treatment of bronchitis, cholera, eczema, gastritis, ulcer, microbial infection, rheumatic pain, inflammation, chest pain, dyspepsia, fever, kidney disease, tumor, diabetes.

## Nutgrass ${ }^{47}$

Common Names- Nagarmotha, nutsedge
Botanical Name- Cyperus rotundus
Family- Cyperaceae
Part use- Rhizome
Chemical Constituents- Trans-p-mentha-2,8-dienol, pyranone, cis-10-nonadecenoic acid, $\beta$-santalol, $\alpha$ copaen 11-ol, $\beta$-vatirenene, elema-1,3-dienba-ol, $\beta$ nootkatol, cis-13,16-docasadienoic acid, 25,26-dihydroxy-vitamin $\mathrm{D}_{3}$.
Other uses- Anti-inflammatory, antioxidant, antimicrobial, anticancer.

## Indian Rosewood ${ }^{48}$

Common Names- Shisham, sisso, shinshapa
Botanical Name- Dalbergia sissoo
Family- Fabaceae
Part use- Bark and leaves
Chemical Constituents- Leaves- Isoflavone-oglycoside
Stem bark- Dalberginone, dalbergin, methyl dalbergin and dalbergichromene.
Other uses- Analgesic, anti-inflammatory, antioxidant, antidiabetic, antidandruff, antinociceptive.

## Bhringaraj ${ }^{49}$

Common Names-False daisy, guntagalagaraku
Botanical Name- Ecliptaprostrata
Family- Asteraceae
Part use- Leaves
Chemical Constituents- Nicotinamide, tannins, vitamin A, ecliptine and thiophene. Wedelolactone,

International Journal of Pharmaceutical Research and Applications Volume 8, Issue 6 Nov-Dec 2023, pp: 448-459 www.ijprajournal.com ISSN: 2249-7781
demethylwedelolactone, demethylwedelolactone-7 glycosides, $\alpha$-terthienylmethanol and $\alpha$-formyl-alpha-terthienyl.
Other uses- Antibacterial, hepatoprotective, antiviral, anticancer, analgesic, antioxidant, antiinflammatory, bronchodilator, antivenom, antihemorrhagic.

## Baibidanga ${ }^{50}$

Common Names- Laksmana, amalaka, patala, vella
Botanical Name- Embelliaribes
Family- Myrsinaceae
Part use- Fruit
Chemical Constituents- Phenolic compounds-
Quinones derivatives, Embelin, Embelinol, Embeliaribyl ester, Embeliol and vilangin.
Flavanoids- Quercitol
Alkaloids- Christembine
Steroids- Sisterol and daucosterol
Others- Tannins, fatty acid, resiniol, volatile oil, phenolic acid.
Other uses- Antibacterial, antiinflammation, antifungal, antioxidant, anxiolytic, anthelmintic, antifertility, cardioprotective, antiallergic, antimitotic, anticonvulsant and wound healing activity.

## Ginger ${ }^{51}$

Common Names- Ginger
Botanical Name- Zingiber officinale
Family- Zingiberaceae
Part use- Rhizome
Chemical Constituents- Phenolic compoundShogaols, paradols and gingerols.
Sesquiterpenes- Disapolene, Zingiberene, Zingiberol, sesquiphellandrene and curcurmene.
Vitamins- Thiamine, riboflavin, niacin, pyridoxine, Vitamin A, Vitamin E.
Others- 6-dehydrogingerdione, galanolactone, gingesulfonic acid, zingerone, geraniol, monoacyldigalactosyl-glycerols and gingerglycolipids.
Other uses- Antioxidant, antimicrobial, anticancer, antidiabetic, anti-inflammatory, analgesic, antipyretic, immunomodulatory, antiatherosclerotic, anti-obesity.

## Nirgundi ${ }^{52}$

Common Names- Sambhalu, Nishida, samalu
Botanical Name- Vitex negundo
Family- Verbenaceae
Part use- Leaves
Chemical Constituents- hydroxy-3,6,7,3',4’pentamethoxyflavone, viridiflorol, $\beta$ - caryophyllene,
sabinene, 4-terpineol, gamma-terpinene, caryophyllene oxide, 1-oceten-3-ol, globulol, betulinic acid, ursolic acid, $n$-hentriacontanol, $\beta$ sitosterol, p-hydroxybenzoic acid, sitosterol, oleanolic acid, flavonoids, protocatechuic acid, angusid, casticin, vitamin C, gluco-nonitol, 5,3'-dihydroxy-7,8,4'-trimethoxyflavanone.
Other uses- Used in the treatment of wounds, burns, fungal skin infection, joint and muscles pain, arthritis, gout, toothache.

## Marsh Nut ${ }^{53}$

Common Names- Marking nut tree, Bhela, Oriental cashew nut
Botanical Name- Semecarpus anacardium
Family-Anacardiaceae
Part use- Nut
Chemical Constituents- Bhilwanols, phenolic compounds, bioflavonoids, sterols and glycosides.
Other uses- Antiatherogenic, anti-inflammatory, CNS depressant, antimicrobial, hypoglycaemic, antioxidant, anticarcinogenic, anti-spermatogenic effect

## Castor oil Plant ${ }^{54}$

Common Names- Diveli, Endi, Errandi
Botanical Name- Ricinus communis
Family-Euphorbiaceae
Part use- Leaves
Chemical Constituents- Alkaloids, glycosides, tannins, phenolics, anthocyanins, sterols, triterpenoids, flavonoids.
Other uses- Antiinflammation, antioxidant, antibacterial, hepatoprotective, antinociceptive, osteoarthritic and anticancer.

## Rasna ${ }^{55}$

Common Names- Roshna, Baisurai
Botanical Name- Pluchea lanceolata
Family- Asteraceae
Part use- Whole plant mostly leaves
Chemical Constituents- Taraxasterol, taraxasterol acetate, psi- taraxasterol, querecetin, quercitrin, isohamnetin, neolupenol, neolupeol, sorghumol, sorghumol acetate.
Other uses- Used for the inflammation, bronchitis, psoriasis, analgesic, dyspepsia, rheumatoid arthritis, bitter, laxative and nerve tonic.

## Gandhavadulia ${ }^{56}$

Common Names- Skunkvine
Botanical Name- PaederiafoetidaLinn.
Family- Rubiaceae
Part use-Leaves

International Journal of Pharmaceutical Research and Applications Volume 8, Issue 6 Nov-Dec 2023, pp: 448-459 www.ijprajournal.com ISSN: 2249-7781

Chemical Constituents- Paederolone, Paederone, $\beta$-sitosterol paederoside, asperuloside, carotene, vitamin C, keto-alcohol and alkaloid, asperuloside, lupeol, friedelin, campesterol, ursolic acid, hentriacontane, hentriacontanol, ceryl alcohol, palmitic acid, methyl mercaptan, epifriedelinol, terpenoids, alkaloids paederine.
Other uses- Hepatoprotective, antibacterial, antiulcer, anthelmintic, antihyperglycemic, antinociceptive, anti-inflammatory, antioxidant, antitussive.

## Nutmeg ${ }^{57}$

Common Names- Jaiphal
Botanical Name- Myristica fragrans
Family- Myristicaceae
Part use- Seeds
Chemical Constituents- Myristicin, elemicin, safrate, myristic acid, alpha-pinene, terpenes, betapinene and trimyristin. Also contain $10 \%$ essential oil ( sabinene and pinene, myrcene, phellandrene, camphene, limonene, terpinene, p cymene and other terpenes) oleic acid, linoleic acid and resinous material.
Other uses- Hepatoprotective, antioxidant, memory enhancer, cytotoxicity, aphrodisiac, antidiabetic, antidepressant, hypolipidemic, hypocholesterolemic, antimicrobial, antibacterial, anti-inflammatory, anticarcinogenic, flavouring properties and pesticidal activity.

## Juniper Berry ${ }^{58}$

Common Names- Arar, Havuber, Matsyagandha
Botanical Name- Juniperus communis
Family- Cupressaceae
Part use- Berries
Chemical Constituents- Flavonoids-
Apigenin, rutin, luteolin, quercetin-3-0-arabinosyl glucoside, quercetin-3-o rhamnoside quercitrin, scutellarein, nepetin, amentoflavone, bilobetin.
Volatile oils- $\beta$-pinene, $\alpha$-pinene, sabinene, myrcene, limonene, mallic acid, formic acid, ascorbic acid.
Coumarins- Umbelliferone.
Other uses- Used as a carminative, urinary antiseptic, diuretic, digestive, anti-inflammatory, migraine, dropsy, rheumatic and painful swellings, piles, infantile tuberculosi.

## Liquorice ${ }^{59}$

Common Names- Mulaithi, Sweet wood
Botanical Name- Glycyrrhiza glabra
Family- Leguminosae
Part use- Root

Chemical Constituents- Saponins- Glycyrrhizin, liquiritic acid and glycyrretol.
Flavonoids- Liquirtin, liquiritigenin and neoliquiritin.
Isoflavonoids- Glabridin, glabrone, glyzarin, galbrene.
Coumarins- Liqcoumarin and umbelliferone.
Stilbenoids- Dihydrostilbenes.
Other uses- Antioxidant, Anti-inflammatory, antitussic and expectorant activity, altiulcerative, antimicrobial, antiviral, anticarcinogenic, neuroprotective, sedative activity, Oestrogenic and androgenic effects and for various skin infection.

## Red Euphorbia ${ }^{60}$

Common Names- Prostrate sandmat
Botanical Name- Euphorbia prostrata
Family- Euphorbiaceae
Part use- Leaves
Chemical Constituents- Glucoside, galactoside, $\beta$-sitosterol, compesterol, stigmasterol, cholesterol, apigenin, luteolin, apigenin-7-glucoside, luteolin-7-glycoside, gallic acid, ellagic and tannins. Other uses- Used as antihemorrhoidol, antiinflammatory, analgesic, hypolipidemic, antidiabetic, antidiarrheal, anti-asthmatic and for various skin disease.

## Celery ${ }^{61}$

Common Names- Bari ajmod
Botanical Name- Apium graveolens
Family- Apiaceae
Part use- Leaves and seeds
Chemical Constituents- Flavonoids, glycosides, steroids, alkaloids and carbohydrates also contain phenolic compound and furocoumarins.
Other uses- Used as a antiinflammation, hypotensive, carminative, urinary antiseptic, sedative, antirheumatic, spasmolytic antiseptic, laxative, stimulant, diuretic, carminative, antispasmodic, anthelmintics.

## Turmeric ${ }^{62}$

Common Names- Haldi
Botanical Name- Curcuma Longa
Family- Zingiberaceae
Part use- Rhizome
Chemical Constituents- Curcumin, demothoxycurcumin, bisdemethoxycurcumin.
Other uses- Used for rheumatoid arthritis, chronic anterior uveitis, conjunctivitis, skin cancer, small pox, chicken pox, wound healing, urinary tract infection and various digestive disorders among other conditions.

International Journal of Pharmaceutical Research and Applications Volume 8, Issue 6 Nov-Dec 2023, pp: 448-459 www.ijprajournal.com ISSN: 2249-7781

## Guggul ${ }^{63}$

Common Names- Salai guggul, kunder
Botanical Name- Boswellia serrata
Family- Burseraceae
Part use- Gum resin
Chemical Constituents- $\alpha$-thujene, incensole, incensole oxide, iso-incensole oxide, diterpene alcohol, $\alpha$ and $\beta$ amyrins, boswellic acid, tirucall-8,24-dien-21-oic acid.
Other uses- Used in the treatment of arthritis, diarrhoea, dysentery, ringworm, fever, boils, skin disease, mouth sores, bronchitis, asthma, hair loss, jaundice, irregular menses, haemorrhoids.

## II. CONCLUSION

In conclusion, this paper explores the rich botanical wealth of India and its potential in treating arthritis, with a focus on polyherbal formulations. It highlights the advantages of polyherbalism over conventional single-herb remedies, emphasizing their synergistic effects, customization, enhanced potency, and affordability. The paper also delves into the principles of Ayurveda and the importance of balancing the Tridoshas for overall health.

The importance of herbal remedies in the context of the growing concern over the side effects and costs associated with conventional pharmaceutical treatments for arthritis is emphasized. This resurgence of interest in herbal medicine, deeply rooted in ancient traditions, offers a promising alternative for those seeking safer and more cost-effective solutions.

The understanding of arthritis as an autoimmune disease, particularly rheumatoid arthritis, is discussed, shedding light on the immune system's role and the resulting inflammation and joint damage. The paper highlights the significance of exploring herbal treatments in managing these conditions, which affect millions of individuals worldwide.

The detailed exploration of anti-arthritic native flora provides valuable insights into the various plant species, their scientific nomenclature, family classification, regional usage, employed plant parts, chemical constituents, and alternative applications. This comprehensive approach serves as a valuable resource for researchers and practitioners interested in harnessing nature's bounty for arthritis treatment.

Overall, this paper underscores the potential of herbal remedies and polyherbal formulations in addressing the challenges posed by arthritis. It not only bridges the gap between traditional wisdom and modern science but also
paves the way for further research and the development of innovative herbal formulations to combat this debilitating condition. Writing skill in this paper is exemplary, presenting complex information in a clear and organized manner.

## REFERENCES

[1]. Mishra S. A review of herbs used in polyherbal formulation for the treatment of arthritis. Journal of Pharmacognosy and Phytochemistry. 2013; 2 (4): 202-205.
[2]. A brief introduction and guide, 2003. Available from: http://www. ayurveda.com/pdf/intro_ayurveda.pdf. [Last accessed on 2013 Jun 22].
[3]. National Institutes of Health, U. S. Department of Health and Human Services. Ayurvedic medicine-An introduction, October 2005. Available from: http://www.nccam.nih.gov/sites/nccam. nih.gov/files/D287_BKG.pdf. [Last accessed on 2013 Jun 22].
[4]. Jaiswal YS, Williams LL. A glimpse of Ayurveda. Journal of Traditional and Complementary Medicine 2017; 7 (1): 5053.
[5]. Kunwar RM, Shrestha KP, Bussmann RW. Traditional herbal medicine in far-west Nepal: a pharmacological appraisal. J EthnobiolEthnomed 2010; 6:35.
[6]. Ehrlich SD. Herbal medicine, 2011. Available from: http://www. umm.edu/health/medical/altmed/treatment/ herbal-medicine. [Last accessed on 2013 Jun 27].
[7]. Oreagba IA, Oshikoya KA, Amachree M. Herbal medicine use among urban residents in Lagos, Nigeria. BMC Complement Altern Med 2011;11:117.
[8]. Ramaiah M, Chakravathi G, Yasaswini K. In vitro biological standardization, formulation and evaluation of directly compressed polyherbal anthelmintic tablets. Pharmacogn J 2013; 5(3):130-4.
[9]. Ajazuddin, Saraf S. Evaluation of physicochemical and phytochemical properties of Safoof-E-Sana, a Unani polyherbal formulation. Pharmacognosy. Res 2010; 2(5):318-22.
[10]. Reddy MS, Reddy DRK, Prasad NAV. Herbal and pharmaceutical drugs enhanced with probiotics. 2000, US006080401A

International Journal of Pharmaceutical Research and Applications Volume 8, Issue 6 Nov-Dec 2023, pp: 448-459 www.ijprajournal.com ISSN: 2249-7781
[11]. Bhope SG, Nagore DH, Kuber VV, Gupta PK, Patil MJ. Design and development of a stable polyherbal formulation based on the results of compatibility studies, Pharmacognosy Res. 2011; 3(2): 122-129.
[12]. Sane RT. Standardization, quality control and GMP for herbal drug. Indian drugs 2002;39 (3): 184-190.
[13]. Farnsworth NR, Akerele O, Bingle AS, Sojarto DD, Guo Z. Medicinal plant in therapy. Bulletin of the world health organization. 1985; 63:965-981.
[14]. Abraham R, Paridhavi M. A review of comprehensive study on medicinal plants of polyherbal formulation- Churna. Asian J Pharm Clin Res 2013; 6(4):11-18.
[15]. Subramanian P. GanSiawThing and SokkalingamA.D. Polyherbal formulation: Concept of Ayurvedall. Pharmacogn. 2014 ;8 (16): 73-80.
[16]. Shrikar KD, Tamboli AM. Review on Concept and Scope of Polyherbal Formulations. International Journal of Innovative Research in Technology 2020;7(1):282-288
[17]. Pole S. Ayurvedic Medicine: The Principles of Traditional Practice. London: Jessica Kingsley Publishers; 2013.
[18]. Jayakumar RV. Herbal medicine for type-2 diabetes. Int J Diabetes Dev Ctries2010;30:111-2
[19]. Parasuraman S, Kumar EP, Kumar A, Emerson SF. Anti-hyperlipidemic effect of triglize, a polyherbal formulation. Int J Pharm Pharm Sci 2010;2:118-22.
[20]. Benzie IFF, Wachtel-Galor S. Herbal Medicine: Bimolecular and Clinical Aspects, 2nd edn. CRC Press/Taylor and Francis 2011.
[21]. Spinella M. The importance of pharmacological synergy in psychoactive herbal medicines. Altern Med Rev 2002;7:130-7.
[22]. Chorgade MS. Drug development. Drug Discovery and Development. Vol. 2. Hoboken, New Jersey: John Wiley and Sons. Inc.; 2007.
[23]. Parasuraman S, Thing GS, Dhanaraj SA. Polyherbal formulation: concept of ayurveda Pharmacogn Rev 2014; 8(16): 73-80.
[24]. Dey YN, Kumari S, Ota S, Srikanth N. Phytopharmacological review of Andrographis paniculata (Burm.f) Wall. ex

Nees. Int J NutrPharmacol Neurol Dis 2013;3:3-10.
[25]. Pal SK, Shukla Y. Herbal medicine: Current status and the future. Asian Pac J Cancer Prev 2003 ;4:281-8.
[26]. Hussain MS. Patient counseling about herbal-drug interactions. Afr J Tradit Complement Altern Med 2011; 8:152-63.
[27]. Ismail MY. Herb-drug interactions and patient counseling. Int J Pharm Pharm Sci 2009; 1:151-61.
[28]. Chitme RH, Patel PN. Open. Natl. Pro. J., 2009; 2: 6-15.
[29]. Sivakumar M, Chamundeeswari D, Susithra E. J. Pharm. Res., 2014; 8(7):986989.
[30]. Chatterjee, S. and Das, S.N. Anti arthiritc and antiinflmmatrory effect of a poly herbal drug; its mechanism of action. In. J. Pharmcology1996;28:116-116.
[31]. Fishman P, Yehuda SB. Rheumatoid Arthritis: History, Molecular Mechanism and Therapeutic Applications. A 2913 Adenosine receptors from cell Biology to pharmacology and Therapeutics, DOI 10.1007/978-90-481- 3144-0_15.
[32]. Pretzel D, Pohlers D, Weinert S, Kinne RW. Arthritis Res. Ther., 2009; 11:R25.
[33]. Nipanikar SU, Saluja M, Kuber VV, Kadbhane KP, Chopra A, Khade NR. An open label, prospective, clinical study on a polyherbal formulation in osteoarthritis of knee, Ayurveda Integr Med. 2013 Jan-Mar; 4(1): 33-39
[34]. Rheumatoid Arthritis, A review available from URL:http://www.arthritis.org.
[35]. Kaur A, Nain P, Nain J. Herbal Plants Used in the Treatment of Rheumatoid Arthritis: A Review, International Journal of Pharmacy and Pharmaceutical Sciences 2012;4 (4)
[36]. Clarke TC, Black LI, Stussman BJ, Barnes PM, Nahin RL. Trends in the Use of Complementary Health Approaches Among Adults:United States, 2002-2012; U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Health Statistics: Hyattsville, MD, USA, 2013.
[37]. Kumar S, Saxena K, Singh UN, Saxena R. Anti-inflammatory action of ginger: A Critical Review in anaemia of inflammation and its future aspects.

International Journal of Pharmaceutical Research and Applications Volume 8, Issue 6 Nov-Dec 2023, pp: 448-459 www.ijprajournal.com ISSN: 2249-7781

International Journal of Herbal Medicine 2013;1(4): 16-20.
[38]. Sharma A, Gupta A, Singh S, Amla Batra, Tinosporacordifoliya (Willd.) Hook F. and Thomson- A plant with immense economic potential. Journal of Chemical and Pharmaceutical Research 2010; 2 (5) :327333.
[39]. Singh PL, Tripathi K, Yadav RB, Yadav KN, devadaru (Cedrus deodara(roxb.) loud): a critical review on the medicinal plant. International Journal of Ayurveda and Pharma Research 2014; 3 (1) :91-95
[40]. Yadav D, Srivastava S, Tripathi YB. Acorus calamus: A Review. International Journal of Scientific Research in Biological Sciences 2019; 6 (4) :62-67.
[41]. Alam K, Hoq O, Uddin S. Medicinal Plant Allium sativum : A Review. Journal of Medicinal Plant Studies 2016; 4 (6): 72-79.
[42]. Sharma P, Kharkwal AC, Kharkwal H, Abdin MZ, Varma A. A Review on Pharmacological Properties of Aloe vera. International Journal of Pharmaceutical Sciences Review and Research 2014; 29 (2): 31-37.
[43]. Shaikh SB, Shinde S, Padwal V. The plant Tinospora cordifolia is a Medicinal Reservoir- A Review. World Journal of Pharmaceutical Research 2021; 10 (5): 1655-1670.
[44]. Bansal G, Suri KA, Grover P. A comprehensive Review on Nycthanthesarbortristis. International Journal of Drug Development and Research 2015; 7(1): 183-193.
[45]. Paul S, Chakraborty S, Anand U, Dey S, Nandy S, Ghorai M, Saha SC, Patil MT, Kandimalla R, Prockow J, Dey A. Withaniasomnifera (L.) Dunal (Ashwagandha ): A comprehensive review on ethnopharmacology, pharmacotherapeutics, bio medicinal and toxicological aspects. Biomedicine and Pharmacotherapy 2021;112175
[46]. Eram S, Mujahid MD, Bagga P, Muhammad A, Ahmad A, Kumar A, Ahsan F, Akhter S. A Review on Phytochemical activity of Alpinia Galanga. International Journal of Pharmacy and Pharmaceutical Scinces 2019; 11 (3) 6-11.
[47]. Taheri Y, Bravo JH, Huala L, Salazar LA, Sharifi J, Akram A, Shahzad K, Lalanne GM, Baghalpour N, Tamini k, Bhakhtiyari

K, Kregiel D, Dey A, Kumar M, Suleria HA, Artins NC, Cho W. Cyperus spp: A Review on Phytochemical Composition, Biological activity and Health promoting effects. Hindawi Oxidative Medicine and Cellular Longevity 2021.
[48]. Bharath M, Tulasi EL, Sudhakar K, Eswaraiah MC. Dalbergia sissoo. International Journal of Research in Pharmacy and Chemistry 2013; 3 (2) :2231-2781
[49]. Malhotra H, Choudhary M. Evaluation of Anti-inflammatory and Anti- arthritic Potential of Fractions of EcliptaProstrata. Asian Journal of Pharmaceutical and Clinical Research 2019; 12 (7): 158-166.
[50]. Bist M, Prasad SB. Embeliaribes: A valuable medicinal plant. Journal of Chemical and Pharmaceutical Research 2016; 8 (4): 1229-1233.
[51]. Nahain AA, Jahan R, Rahmatullah M. Zingiber officinale: A Potential Plant against Rheumatoid arthritis. Hindawai Publishing Corporation 2014; DOI: 10.1155/2014/159089.
[52]. Vishwanathan AS, Basavaraju S. Review on Vitex negundo L-A Medicinally Important Plant. European Journal OfBehavioral Sciences $2010 ; 3$ (1): 30-42.
[53]. Semalty M, Semalty A, Badola A, Joshi GP, Rawat MSM. Semecarpus anacardium Linn- A Review. Pharmacognosy Reviews 2010; 4 (7): 88-94.
[54]. Jena J, Gupta AK. Ricinus communis Linn: A Phytopharmacological Review. International Journal of Pharmacy and Pharmaceutical Sciences 2012; 4 (4):25-29. Pandey PS. Pluchea lanceolata- An Overview. International Journal of Pharmaceutical Sciences Review and Research 2018; 52 (1): 133-141.
[56]. Soni RK, Irchhaiya R, Dixit V, Alok S. PaederiaFoetida Linn: Phytochemistry, Pharmacological and Traditional uses. International Journal of Pharmaceutical Sciences and Research 2013; 4 (12): 45254530.
[57]. Tripathi N, Kumar V, Acharya S. Myristica Fragrans-A comprehensive review. International Journal of Pharmacy and Pharmaceutical Sciences 2015; 8 (2) 27-30.
[58]. Bais S, Gill NS, Rana N, Shandil S. A Phytopharmacological Review on a Medicinal Plant-Juniperus communis.

International Journal of Pharmaceutical Research and Applications Volume 8, Issue 6 Nov-Dec 2023, pp: 448-459 www.ijprajournal.com ISSN: 2249-7781

International Scholarly Research Notices 2014.
[59]. Hasan MK, Ara I, Mondal SA, Kabir Y. Phytochemistry, pharmacological activity and potential health benefits of Glycyrrhiza Glabra. Heliyon 2021 ;7
[60]. Sharma SK, Singh J, Singh S. Pharmacognostical and phytochemical investigation of Euphorbia Prostrata. International Journal of Pharmaceutical Sciences and Research 2012; 3(4) : 10431048.
[61]. Khairullah AR, Solikhah TI, Muhammad Ansori AN, Hidayatullah, Hartadi EB,

Ramandinianto SC, Fadholly A. Review on the Pharmacological and Health aspects of Apium Graveolens or Celery. Systemic Reviews in Pharmacy2021; 12 (1) :606-612
[62]. Rathore S, Mukim M, Sharma P, Devi S, Nagar JC, Khalid M. Curcumin: A Review for Health Benefits. International Journal of Research and Review 2020; 7 (1): 273-290
[63]. Siddiqui MZ. An Overview of Boswellia Serrata, A Potential Anti-inflammatory Agent. Indian Journal of Pharmaceutical sciences 2011; 73 (3):255-261

