



DEVELOPMENT AND EVALUATION OF HERBAL FORMULATION FOR RHEUMATOID ARTHRITIS: An Research.

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ABSTRACT:

Osteoarthritis, also known as degenerative joint disease is the most common form of Arthritis. The most common types are osteoarthritis & rheumatoid arthritis both osteoarthritis. A bio-mechanical and inflammatory disease influenced several factors such as mechanical & oxidative stress injury, age, obesity, and metabolic disease OA is characterized by joint cartilage degeneration, changes in the underlying bone, and cytokines, pro-inflammatory and pro-catabolic mediators are found localized in Synovial fluid and such as matrix metalloproteinases, are associated with cartilage degeneration. The use of herbal medicine in the treatment of RA is as old as humanity and civilization.

Keywords: Rheumatology osteoarthritis, cartilage degeneration, pro-catabolic mediators, humanity.

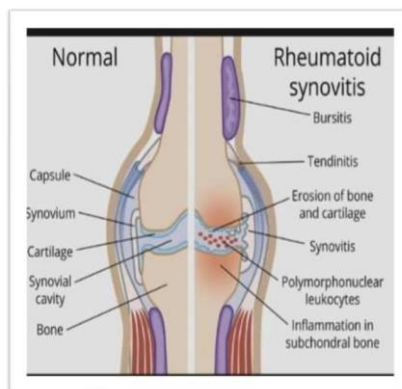
Introduction:

Arthritis is a common health issue that affects millions of people in the United States. Patients suffering from Arthritis struggle with several joint pains & nearly half of all adults with arthritis experience persistent pain. More than 100 types of arthritis have been identified. Two of the most common types are osteoarthritis & rheumatoid arthritis both osteoarthritis. Osteoarthritis and rheumatoid arthritis impair joint structure and function but differ in symptoms, pathophysiology, and treatment.

Pathophysiology of Rheumatoid Arthritis:

Chronic inflammatory disorder of autoimmune origin principally attacks the joints, producing a non-suppurative proliferative and inflammatory synovitis, articular lesions, distribution of the articular cartilage, and in some cases ankylosis of the joints. Extra-articular lesions may occur in the skin, heart, blood vessels, and lungs. Causes of symmetrical polyarthritis affect several joints in pairs on both sides of your body.

- Epidemiology
- Etiology
- Morphology



Features Include:

- 1) Synovial cell hyperplasia and proliferation.
- 2) Dense inflammatory infiltrates of CD4 + helper T cells, B cells, plasma cells, dendritic cells, and macrophages.
- 3) Increased vascularity resulting from anti-agenesis.
- 4) Neutrophilic aggregates of organizing fibrin on the synovial and joint surfaces.
- 5) Osteoclastic activity in underlying bone, allowing the home synovium to penetrate into the causing periarticular erosions and subchondral cysts.

Herbs used in Rheumatoid Arthritis:

1) Ginger:

Synonym :- Gingerin, Rhizoma Zingiberis, Zingiberis, Ginger officinale.

Family :- Zingiberaceae

Biological source:-The ginger is the rhizomes of zingiber officinale Roscoe & dried in the Sun



Chemical constituent: Ginger exhibit a vital role to lessen the unbearable pain & inflammation associated with. RA ginger is obtained from rhizomes. It has been widely used as a medicinal herb & spice. since ancient times. Anti-inflammatory effect of ginger was scientifically proved first by kiuchi in 1982. They isolated four new different compounds from ginger, and all showed the potential inhibitory effect to reduce prostaglandin synthesis, which is the key to Inflammation. Active components include gingeals, gingerdials and gingerdions and their dehydration products The shagaols. officinale black inflammatory prostaglandins and thromboxane.

2) Turmeric:

Synonyms :- Saffeen, Indian Haldi, curcuma Rhizoma

Biological Source:-Turmeric is the dried rhizome of curcuma longa Linn.

Family:- Zingiberaceae



Chemical constituents: Turmeric contains yellow coloring matter called as acuminoid (s) and essential oil (6x). The chief constituent of the coloring matter is curcumin I (607), addition with small quantities of curcumin, T Curarmin I and date Curcumin The volatile oil contains mono- and sesquiterpenes like Zingiberene arturmerone Beeneel and cineole choleric action of the essential oil is attributed to p-tolylmethyl cinnel.

3) Nirgundi:

Synonym: Chaste tree, man ching, Negundo, lengund..

Family:- Lamiaceae.

Biological Source: It is obtained from the leaves of plant Vitex Negunda.



Chemical constituents: Carbohydrates, sterols, C-glycosides, Flavonoids, Polyphenolic compounds, terpenoids, glycosidiaridoids & alkaloids, Casticin, Essential oil, Benzoic acids, vitamin-C, Flavones; 3P-Acetyroyleon-12-en-27-oic acid, 2 α ,3 α -diacetoxyolean-5,12-dien-28-oic acid; 2 β , 3 α -dihydroxyolea-5,12-dien-12-28-oic acid & 2 α ,3 β -diacetoxy-18-hydroxyolean-5,12-dien-28-oic acid isolated from seeds. It is a hardy plant, flourishing mainly in the Indian region. It has analgesic, anti-bacterial and anti-inflammatory properties. It is useful in the treatment of fever, arthritis, headaches, swelling, digestion problems and mouth related problems. The Sub-effective dose of Nirgundi potentiated.

4) Gokshur Churna:

Synonym: Bada Gokhru (Big Gokhru) and Chota Gokhru (Small Gokhru), Brihat gokshur (Sanskrit), Bada goshur (Hindi) Yenugu palleru (Telugu), Puncture vine, Devil's weed, Large caltrops.

Family:- Tribulus terrestris or Zygophyllaceae.

Biological Source: The smaller or Chhota Gokhru is the dried ripe seeds of Tribulus terrestris Linn.



Chemical constituents: Alkaloids 3.5%–5%, stable oil, aromatic oil, resins, glycosides, carbohydrates, saponins and triterpenoids. Stem: Saponins, herman, phytosterols, tannins and carbohydrates. Root: Reducing sugars, phenolic compounds, saponins, xanthoproteins, alkaloids, triterpenoids and flavonoids.

5) Licorice:

Synonyms :- Sweet Licorice, Radix alcyrrhizae.

Family: - fabaceae.

Biological Source :-Licorice consists of subterranean peeled and unpeeled tubers Roots and stems of *Glycyrrhiza glabra* Linn and other species of *Glycyrrhiza*. Belonging to family Leguminosae.

Chemical constituent :- *Glycyrrhiza glabra* (licorice) is a herb belonging to the pea and bean family, licorice is cultivated for its underground stems that are used to flavour confectionery; it is also valued for its medicinal qualities. In the traditional system of medicine, the roots and rhizomes of *Glycyrrhiza glabra* (Family: Leguminosae) have been employed clinically for centuries for their anti-inflammatory, antiulcer, expectorant, antimicrobial and anxiolytic activities. In modern medicine, licorice extract has been used for peptic ulcer and as an alternative to bismuth that has a protective role against acid and pepsin secretions by covering the site of lesion and promoting the mucous secretion. There are many useful compounds in licorice root such as, glycyrrhizin and its aglycone, glycyrrhetic acid which are clinically used for hyperlipidemia. Licorice flavonoid constituents mainly include flavones, flavonols, isoflavones, chalcones, bihydroflavones and bihydrochalcones. A pharmacological investigation indicates that they have antioxidant, antibacterial and anti-inflammatory activities.



6) Thyme:

Synonym: *Thymus vulgaris*.

family: Lamiaceae (mint).

Parts used: Aerial parts.

Emergetics: pungent' hot.



Plant properties: Antimicrobial, carminative, Stimulating/ relaxing diaphoretic, antispasmodic, expectorant, emmenagogue, vermifuge.

plant uses: Infection, symptoms of cold and influenza (fevers sore throat, cough), UTI infections, wound, mouth wash, thyme is the most widely used herbal medicine among patient Rheumatoid Arthritis. Thyme also has antimicrobial and anti-inflammatory properties that can be therapeutic for Rheumatoid Arthritis.

7) Cinnamon:

Synonyms :- Dalchini, ceyton cinnamon, cinnamon.

Family: Lauraceae.

Biological source :- Cinnamon consists of dried bark free for the outer cork and from underlying parenchyma, from the shape of growing on the cut stumps of *Cinnamomum zeylanicum* Nees.

Chemical Constituent :- Essential oil (5 to 20 ml/kg) is composed of phenylpropane derivatives cinnamon oil mainly contains Cinnamaldehyde (60 to 70 %) benzaldehyde Cinnamaldehyde and other terpenes such as pinene, cymene.



MATERIAL AND METHOD:

Plant materials:

i) *Vitex negundo* (Nirgundi)

ii) Xanthium (Gokhru)

iii) Liquorice

Preparation of extract: Air dried and coarsely powdered of Nirgundi , Gokshur churn and liquorice in the thimble made up of filter paper and it place inside the Soxhlet apparatus. The apparatus is fitted to the round bottomed flask containing the solvent and to a reflux condenser. The solvent in the RB flask is boiled the vapour passes through the side tube condensed by the condenser and fall into the thimble containing the material or herbal drug. In RB flask , the extract is collected with high amount of alcohol to remove the alcohol quantity boiled it. Due to this alcohol get separated and herbal extract are remaining in the flask.



Fig. Schematic of a Soxhlet extraction apparatus indicating the vapor and liquid extractant paths. The sample under extraction is cushioned by loosely packed ceramic fibers.

Cream Formulation:

- 1) first weigh the accurate quantity of chemical, as given in the formula.
- 2) The vitexnegum. (Nirgundi), Xanthium (Gokhru) and liquorice are taken in first beaker.
- 3) Then heat on waterbath for uniform mixing, After few minutes oil phase was formed.
- 4) Distilled water, white soft paraffin borax, methyl Paraben, and propyl paraben in second beaker Mixing all ingredients by Heating on water bath.
- 5) The aqueous phase was formed oil phase was added into aqueous Phase.
- 6) continuous stirring was done untill Semisolid mass was formed.
- 7)Smooth consistancy of cream is maintained by rubbing spatula.
- 8) The formed cream is ready for evaluation.



Fig. Cream for Rheumatoid Arthritis

Table: Formula for Cream formulation:

Sr.No.	Ingredients	Quantity
1.	Vitexnegum	1 gm
2.	Xanthium	1 gm
3.	Liquorice	1 ml
4.	Bees wax	3.2 gm
5.	White soft paraffin	12 ml
6.	Borax	0.03 gm
7.	Methyl paraben	0.03 gm
8.	Propyl paraben	0.02 gm
9.	Distilled water	Qs
10.	Menthol	Qs

Evaluation test:

Formulated herbal cream was further evaluated by using the following physical parameter Colour, odour, consistency State of the formulation

a) Colour : The colour of the cream was observed by visual examination. The cream is in green colour.

b) Odour: The to be odour of cream was found to be Characteristics.

c) State: The state of Cream was examined visually. The cream was solid in state.

d) Consistency: The formulation was examines by rubbing cream on hand manually. The cream having smooth consistency.

e) Ph: Ph of prepared herbal cream was measured by using digital ph meter. The solution of cream was prepared by using 100 ml of Distilled water and set aside 2h. Ph was determined in three times for solution and the average value was calculated.

f) Spreadability: spread ability of formulate cream was measured by placing sample in between two slides then compressed to uniform thickness by placing a definite weight for defined time. The specified time required to separate the two slides was measured as Spreadability. Lesser the time taken for separation of two slides results showed better Spreadability. Spreadability was calculated by the following formula-

$$\text{Spreadability(S)} = \frac{\text{Weight tide to upper slide(W)} \times \text{Length of glass slide(L)}}{\text{Time taken to separate slide(T)}}$$

g) Viscosity measurements. The viscosity (in eps) of the products was measured using a Brookfield Viscometer (Brookfield, MA) The spindle was spun at a speed of 2.5 revolutions per minute. Before the analyses, the cream specimens were permitted to stay for 30 minutes at the specified temperature (25+1[^]{circ}C).

h) Stability analysis: Temperatures of 10°C, 30°C, and 45°C were used to keep the composition. For four

weeks, the viscosity, pH, and appearance of the specimens were monitored.

i) Toxicity test: The toxicological tests were carried out for a total of 28 days.

j) Skin irritation test: Herbal creams A with varying concentrations of herbal preparation were applied to the epidermis. The sample cream and the swab carrying it has adhered to the treated area with adhesive strips. Then any erythema was detected and assessed according to the application site's state. Severe erythema, Moderate erythema, Slight erythema, Or No imitation.

k) Washability: formulation was applied on the skin and then ease extends of washing with water was checked.

RESULT:

Results for rheumatoid arthritis cream:

Sr.No.	Parameter	Result
1.	Colour	Green
2.	Odour	Characteristics
3.	State	Semisolid
4.	Consistency	Smooth
5.	Spredability	7.2 g.cm/cm
6.	Washability	Easy washable
7.	Skin irritation test	Non-irritant
8.	Toxicity test	Non-toxic
9.	Stability analysis	Stable
10.	Ph	6.6

SUMMARY:

Rheumatoid arthritis is a common autoimmune disease that can lead to serious functional limitations, joint destruction, extra-articular disease, poor quality of life, and premature death Early recognition of arthritis and speedy referral to a rheumatologist are essential Treatment should start early and aggressively to prevent functional limitations and structural damage Innovations in treatment and monitoring have resulted in patients achieving early and sustained clinical and radiographic remission Methotrexate is the first line drug, but in high risk patients early combination of methotrexate with prednisone or a tumour necrosis factor inhibitor improves outcomes.

CONCLUSION:

SRA is a chronic disease that requires interventions to modify disease progression. While initial presentations are related to joint inflammation, long-term sequelae can include extra-skeletal manifestations. The most recent RA guidelines are from ACR 2015 and EULAR 2016. There are specific differences between the guidelines, based on the respective region/population studied. A future update of the ACR guidelines may contain commentary regarding the roles of baricitinib and sarilumab, as well as other promising therapies.

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