

**ABSTRACT**

**Aim: Pharmacological evaluation of some herbs in experimentally induced Rheumatoid arthritis along with cardiovascular complications.**

**BACKGROUND:** The prevalence of cardiovascular complications (CVD) in patients suffering from Rheumatoid arthritis (RA) is one of the major concerns today which is associated with both morbidity and mortality. There are two main reasons of occurrence of CVD in RA: The first being inflammation driven by TLR receptor activation, works as underpinning factor in both the diseases and second one is the side effects and drawbacks of existing therapies. According to the European League Against Rheumatism (EULAR) and FDA the drug regimen (NSAIDs, DMARDs) of RA also contributes in progression of CVD. Moreover there is no such animal model developed till date which gives a complete insight of CVD in RA. The proposed hypothesis is divided in to two stages one will be the development of animal model replicating CVD in RA using **Lipopolysachcharide (LPS)** and **High Fat Diet** with **CFA** and **collagen**. The aim of model is to activate TLR -4 receptors releases during **immune responses, inflammation, RA and CVDs**. HFD and LPS activates TLRs, these trigger factor are highly expressed proteins in the synovial lining and sub lining layer of RA synovium and cardiac muscles. TLRs process endotoxemia, infiltrate the cells and stimulates cytokines like **TNF- $\alpha$ , IL-6, IL-8, and NF- $\kappa$ B** responsible for CVD in RA. In second stage formulations will be developed by the potential of using medicinal herbs as anti arthritic drug is promising to increase life expectancy and patient compliance in long term diseases like arthritis. Deep literature survey reveals anti arthritic and cardio protective properties of *Nigella sativa* seed, *Carica papaya* seed and *Momordica charantia* seed. *Nigella sativa* is commonly known as Kalonji contains Thymoquinone possessing anti inflammatory, anti arthritic, anti Atherogenic which corrects endothelial dysfunction and inhibits TNF- $\alpha$  production. *Carica papaya* seed commonly known as paw-paw seed is categorized as super food, flavanoids are major constituent with analgesic, anti inflammatory, wound healing and cardio protective properties. *Momordica charantia* (Karela or bitter gourd) having account of anti inflammatory and wound healing properties due to presence of flavanoids. Thus the objective of the study is to optimize an herbal formula containing *Nigella sativa*, *Carica papaya* and *Momordica charantia* seed by establish its efficacy in a validated model in RA with CVD complications.

**MATERIAL AND METHODS:** In first part of study model development with two different

inducing agents; CFA and CIA was performed to check the development of Rheumatoid Arthritis in wistar rats. The study was further carried out to establish CFA and collagen induced Rheumatoid Arthritis along with cardiovascular complications by diet modification (HFD) and LPS sensitization. Evaluation was done for model validation by applying predictive validity (graded for pharmacological parameters Neutrophil count, CRP, ESR, Anti-CCP, IL-6, TNF- $\alpha$ , RF Factor), face validity (graded for core symptoms; Paw volume, Arthritic score, Arthritic index, X Ray, histopathology) and constrict validity (graded for disease similarities and human resemblance; pain, symmetrical secondary lesions, digestion of digits, steatosis, Homocysteine levels and co morbidities) to compare the pharmacological actions. Ameliorative effect of *Nigella seed*, *Carica papaya seed* and *Momordica charantia seed* aqueous extract was evaluated in this study against CFA and Collagen induced Rheumatoid Arthritis alone and also for cardiovascular complications stimulated via Rheumatoid Arthritis as extra articular manifestation.

**RESULTS:** CFA and CIA induced Rheumatoid Arthritis model along with HFD and LPS shown the initiation of cardiovascular disorders and the severity index was indicated the higher etiological changes in CIA induced groups. Ameliorative effect of combination of *Nigella seed*, *Carica papaya seed* and *Momordica Charantia seed* aqueous extract were proved to possess protective effects against RA and CVD complications in different doses.

**CONCLUSIONS:** Sensitization of LPS in 10  $\mu\text{g/ml}$  dose along with high fat diet and collagen caused cardiovascular complications in and the disease severity was noticed in this Collagen 0.1ml +HFD+LPS 10  $\mu\text{g/ml}$  group evident from face validity, constrict validity and predictive validity parameters. Treatment regimen of combination of aqueous extracts of *Nigel sativa seed* (200 mg/kg, p.o.), *Carica papaya seed* (50mg/kg p.o.) and *Momordica Charantia seed* (400mg/kg p.o) was found to give prevention against cardiovascular complications in RA as evident from decrease in inflammation, decrease in immunological response, The results were comparable to MTX in decreasing inflammation and immunological responses and significant in amelioration of cardiovascular complications.