# ABSTRACT

Inflammation is the immediate response of the host body against any incoming pathogen. The different immune cells and immunological molecules contribute to the inflammatory process which leads to the killing or elimination of the pathogen from the host body. If the inflammation persists beyond the immediate onset after the elimination of the pathogen, it can harm the host body locally or systematically. Inflammatory diseases like Rheumatoid Arthritis (RA) occur when the resolution of inflammation is delayed or disturbed. RA is a common multi-factorial disease found globally at a frequency between 0.5 – 1% of the total population. RA-like multi-factorial diseases lack satisfactory treatment remedies which can cure the disease from the root. The drugs used in the present medicinal system generally inhibit or suppress the inflammation and the disease flares up whenever there is a discontinuation in treatment process. These medicines also have various side-effects. In the complementary and alternative medicinal systems (CAM), the evidence-based evaluation of different herbal remedies are assessed which can be used as an additional aid to the patients of RA-like diseases leading to the amelioration of the health. These therapies generally have minimal or no side-effects. About 70% of the people directly or indirectly rely on CAMs for the betterment of their disease condition.

The plant *Aloe vera* is one of the most explored plants world-wide which has been used as food, as well as in pharmaceutical industries. It is often used as laxative, consumed and topically used in pain-reduction, against inflammation, burn and in other injuries in gamut of the herbal medication system. This plant naturally grows in all the tropical and sub-tropical countries, including in India. Often termed a “miracle plant”, the use of its medicinal properties has been well documented in the ancient civilizations and by the ethnic communities all through the World. However, it is evident that most of the anti-inflammatory activities of the plant are not scientifically well-proven and the ethnic documentations are not supported by strong scientific base.

In the present study, the crude unprocessed aqueous homogenized *Aloe vera* leaf has been used as the subject herbal resource. The anti-inflammatory activities of the plant gel as well as the anti-rheumatic properties of the gel have been explored in detail in this dissertation work. The common use of the *Aloe vera* gel in joint pains by the local people of the sub-Himalayan

region was assessed scientifically. The consumption of the gel by the common people, in a crude and unprocessed condition following a fresh collection, has been the major cues for determining the strategies and doses of the plant gel in *in vivo* and *in vitro* studies. The toxicological properties of the gel at their consumable doses in model animals were also assessed in the process.

The freshly prepared *Aloe vera* gel homogenate was used as an oral remedy in different experiments, which was a novel approach for the determination of crude gel properties without any extraction process. Animal model-based *in vivo* studies as well as *in vitro* studies have been undertaken to find the acute and sub-chronic toxic role of gel constituents. *In vitro* models of inflammation were prepared following RBC membrane stabilization assays against heat-induced and hypotonicity-induced stress generation; and protein denaturation-inhibition assays were done. *In vivo* inflammatory models like carrageenan-induced paw-swelling models and cotton pellet-induced granuloma models in Wistar rats were standardized; *in vivo* anti-arthritic assessment was done in Freund's complete adjuvant (FCA)-induced arthritic rat models. *Aloe vera* gel up to a dose of 0.80 g kg body weight of model animals were orally supplemented in the animal models of inflammation and inflammatory arthritis. Different physiological properties and parameters were studied and the benefits of orally-consumed *Aloe vera* leaf gel were assessed after the induction appropriate inflammatory or arthritic conditions in animal models. The relative expression analyses of some major genes involved in inflammation, as well as rheumatoid arthritis, was done through real-time quantitative PCR to explore the further reasons of such initial findings. The significant *Aloe* gel constituents were also identified using the available scientific reports and were used for the assessment of their individual efficacy through sophisticated *in silico* computer simulation techniques.

It was observed that the crude *Aloe vera* gel homogenate did not show any acute toxic effect up to the dose of 5g/kg body weight and sub-chronic toxic effect up to 4g/kg body weight in experimental rat models. In the cotton pellet-induced granuloma and carrageenan-induced paw-swelling animal models, animals showed a decrease in their inflammatory response when treated with *Aloe vera* gel homogenate orally. In the FCA-induced arthritic model, the arthritic swelling, hematological, and serum biochemical parameters were brought back to normalcy. Expression of cytokines like TNF-α and immunomodulatory genes like Cox-2 which increases

during RA were also down-regulated in FCA-induced arthritic model animals following the *Aloe vera* gel oral supplementation, provided daily for a period of 28 days. The findings were explained and corroborated in a detailed way so that the probable pathways for the inflammation and arthritis inhibition, done by the *Aloe vera* gel, could be revealed. All the findings have been published as research articles in reputed journals.

It can be concluded from the findings of the dissertation that, the Aloe vera leaf gel homogenate can inhibit the inflammatory disease-conditions in the experimental model systems and the efficacy of the gel can open opportunities for the establishment of new CAM therapy against inflammation. The gel did not show any toxic effect as well, so the consumption of the gel is devoid of any possible side-effects.