

# Pharmacological Evaluation of Manilkara Zapota (L.) P. Royan Fruit Peel Extract for Anti- Inflammatory Effect and Antioxidant Activity in Experimental Animals

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**Abstract:** *Background: Manilkara zapota (L.) P. Royen is commonly known as Chiku, belonging to the family Sapotaceae which is native to Mexico and central America and widely distributed in tropical and subtropical regions of Asia, Brazil and Australia. Manilkara zapota is a medicinal plant, various parts of this plant are traditionally used for treatment of several diseases, including analgesic, antipyretic, anti-diabetic, antioxidant, anti-inflammatory, and diuretic activity. The plant has been widely used in traditional systems of medicine in India.*

*Aim: Present investigation was undertaken aimed at "Pharmacological Evaluation of Manilkara zapota (L.) P. Royen fruit peel extract for Anti-inflammatory Experimental Animals." Method: Ethanolic extract of Manilkara zapota fruit peel was subjected to continuous hot extraction by Soxhlet extraction process using ethanol (80%) as a solvent. Preliminary phytochemical evaluation of ethanolic extract was carried out for the determination of presence of phytoconstituents. The in-vitro Anti-inflammatory activity was evaluated by Heat induced hemolysis and Inhibition of albumin denaturation assay. and Antioxidant activity was evaluated by DPPH radical scavenging assay.*

*Result: The result suggested that the Phytochemical screening of ethanolic extract reveals the presence of alkaloid, flavonoid, carbohydrates, Tannin, phenol and saponin in Preliminary phytochemical evaluation. The in-vitro antioxidant activity revealed with the ethanolic extract Manilkara zapota at the concentrations 50, 100, 150, 200 µg/mL exhibits 65%, 68%, 78%, 81% radical scavenging activity, whereas the As c o r b i c a c i d a s a standard drug at concentration 50, 100, 150, 200 µg/mL exhibit 71%, 79%, 84%, 89% radical scavenging activity respectively by using DPPH radical scavenging assay. In-vitro Anti-inflammatory activity reveals with the ethanolic extract of Manilkara zapota at concentration 50, 100, 150, 200 µg/ml exhibit 33%, 39%, 48%, 57% inhibition, whereas the Diclofenac as a standard drug at concentration 50, 100, 150, 200 µg/ml exhibit 45%, 54%, 69%, 78% inhibition of erythrocyte membrane respectively by using Heat induced hemolysis assay. While In- vitro Antiinflammatory activity revealed with EEMZ at concentration 100, 200, 300, 400 µg/ml exhibit the 63%,66%,80%,85% inhibition respectively whereas Diclofenac as a standard drug at concentration 100, 200, 300, 400 µg/ml exhibit the 67%, 80%, 86%, 90% inhibition respectively by using Inhibition of albumin denaturation assay. Conclusion : The study concluded that the antioxidant and Anti-inflammatory effects of Manilkara zapota Royen fruit peel extract that exhibit due to the presence of some phytoconstituents such as flavonoids, phenol, tannins, carbohydrates, alkaloids, saponin, carbohydrates ,amino acids as revealed in literature..*

**Keywords:** antiinflammatory drugs.

## I. INTRODUCTION

### Inflammation

#### Definition

"Inflammation is the pathophysiological complex biological response of living mammalian tissues to harmful stimuli or injuries including pathogens, irritants or damaged cells that leads to the local accumulation of plasma fluid and blood

cells.” (Amlan G. *et al.*, 2013) (S. Shukla *et al.*, 2009). It is a protective attempt by the organism to remove the injurious stimuli as well as initiate the healing process for the tissue. Inflammation, however, if runs unchecked, led to onset of diseases such as vasomotor rheumatoid arthritis, atherosclerosis (Juvekar *et al.* 2009). The complex events and mediators involved in the inflammatory reaction can induce, maintain or aggravate many diseases. However, studies have been continuing on inflammatory diseases and the side effects of the currently available anti-inflammatory drugs pose a major problem during their clinical uses. Therefore, development of newer and more substantial antiinflammatory drugs with lesser side effects is necessary. (S. Shukla *et al.*, 2009).

Inflammation is a major component of the damage caused by autoimmune diseases, and is a fundamental contributor of various infectious and non-infectious diseases such as cancer, diabetes, cardiovascular disease, rheumatoid arthritis, Alzheimer’s and arteriosclerosis. Depending on the intensity of this process, mediators generated in the inflammatory site can reach the circulation and cause fever (Lucas *et al.*, 2006).

Acute and chronic Inflammatory diseases remain one of the world’s major health problems. It involves a complex array of biochemical process such as enzyme activation, inflammatory mediator release and extravasations of fluid, cell migration, and tissue damage and repair. (A. A. Tamiru *et al.*, 2018).

NSAIDs drug are among the most commonly prescribed drugs due to their consistent effectiveness in the treatment of pain., fever, inflammation and rheumatic disorders. However, their use is associated with adverse effects at the level of digestive tract, ranging from dyspeptic symptoms, GIT erosions and peptic ulcer to more serious complication, such as over bleeding. (Md. H. Hossain; F. Jahan *et al.*, 2012).

Inflammation is a complex pathological process mediated by a variety of molecules produced by leucocytes, macrophages and mast cells undergoing various cellular responses such as phagocytic uptake, and the production of inflammatory mediators such as nitric oxide (NO), prostaglandin E2 (PGE2) and tumour necrosis factor (TNF)- $\alpha$  (Kinne *et al.*, 2000), that bring about formation as a result of extravasation of fluid and proteins and accumulation of leucocytes at the inflammatory site (White *et al.*, 1999).

Inflammation diseases including, different types of rheumatic diseases are the major problems associated with the presently available anti-inflammatory agents. The no. of plants derived drugs have been screened for their anti-inflammatory, analgesic activity antioxidant activity. (S. H. Nile; Se Wonpark *et al.*, 2013). Inflammation is a finely tuned, process, and its dysregulation underlies many complex diseases (e.g., sepsis, infectious diseases trauma, allergy, autoimmune disorders, transplant rejection, cancer, neurodegenerative diseases, obesity and atherosclerosis). Inflammatory processes are required for immune surveillance, optimal repair, and after injury (Vodovotz *et al.*, 2008). Inflammation is an important cellular response triggered by various mechanical, chemical or immunological stress factors and it is regulated by a delicate balance between local factors that finally determine the outcome of the disease process: progression or resolution. The inflammatory response is a complex and highly regulated sequence of events that start with an initial production of pro- inflammatory mediators that recruit professional inflammatory cells to the site of injury to clear the off trigger. This is followed by an antiinflammatory phase, in which resident tissue cells may acquire the potential for protecting themselves from further activation and injury (Huwiler *et al.*, 2009).

The NSAID are among the most commonly prescribed medication worldwide. They consist of a group of drugs that are used in fever, pain, and inflammation because these drug anti pyretic, analgesic and anti-inflammatory properties Clinically, they are useful in relieving pain in many conditions, to arthritic pain. These drugs are well known agents, and they exert their effects through the inhibition of prostaglandin synthesis by blocking the enzyme (COX). (Rebecca S.Y. Wong *et al.*, 2019).

### **Mechanism of action of inflammation**

Mechanism of inflammation represents a chain of organized, dynamic responses including both vascular and cellular events with specific humoral secretions. These pathways involve changing physical location of white blood cells (monocytes, basophils, eosinophils, and neutrophils), plasma, and fluids at inflamed site. A group of mediators and other molecules (e.g., histamine, leukotrienes, oxygen- and nitrogen-derived free radicals, and serotonin) are released by immune cells principally in the mechanism which can contribute in the event of inflammation.

Whatever, the inflammatory response is triggered by two phases: (a) acute and (b) chronic and each is mediated by a different mechanism These immune responses which involved in acute inflammation can be divided into vascular and

cellular inflammation. The responses which occur in microvasculature normally appear in few minutes following tissue injury or microbial infection in the presence of other inflammatory stimuli named vascular events. The occurrence of these processes is rapid and eventually will lead to vasodilation and subsequently makes the vessels become more permeable. processes will result in entry of inflammatory mediators and produces interstitial (L. A. Abdul et al.,2018).

Understanding inflammation has always been an enigma for mankind. something as minor as a bruise or something as major as a myocardial infraction can trigger this phenomenon. The major class of drug to suppress inflammation are nonsteroidal agent (NSAID) and corticosteroid but their toxic adverse effects such as epigastric distress, peptic ulceration, osteoporosis, and iatrogenic Cushing’s syndrome have limited their use. Looking at the present scenario, medicinal compounds derived from plants sources such as flavonoids, saponins, alkaloids, terpenoids, glycosides, coumarins could provide an excellent fountainhead to develop new anti-inflammatory agents, which could be more efficacious, safe, affordable, and accessible for patients. (G.G. Meshram et.al.,2014).

Modulation of inflammatory reaction can be on various level targeting different cell types. first inflammatory cell including the monocytes /macrophages, neutrophils, etc.

may be targeted. This includes; (1) inhibition of immune cell activation which leads to a reduced production and secretion of pro- inflammatory cytokines and chemokines. (2) reducing chemotaxis of immune cells by blocking the production, secretion or action of chemotactic factor (3) blocking the interaction of immune cell with vessel end cells and therapy reducing the extravasation of immune cells into the inflamed tissue. (4) Blocking eicosanoid production in immune cells and tissue resident cells to reduce the cardinal symptoms of inflammation. (5) Activation of anti-inflammatory signaling cascade in immune cells and resident tissue cells to actively counteract and resolve an inflammatory reaction. (Huwiler et al., 2009).

Research on the biological activities of plants during the past two centuries has yielded numerous compounds for the development of modern drugs. (Juvekar et al.2009).

The inflammatory pathway it consists of inducers, sensors, mediators, and target tissues. Inducers initiate the inflammatory response and are detected by Sensors, such as Tolllike receptors (TLRs), are expressed on specialized sentinel cells, such as tissue resident macrophages, dendritic cells, and mast cells. They induce the production of mediators, including cytokines, chemokines, bioactive amines, eicosanoids, and products of proteolytic cascades, such as bradykinin. These inflammatory mediators act on various target tissues to elicit changes in their functional states that optimize adaptation to the noxious condition (e.g. infection or tissue injury) associated with the particular inducers that elicited the inflammatory response. The specific components shown represent only a small sample of the myriad different sensors, mediators, and target tissues involved in the inflammatory response.

(Medzhitov Z. et al. 2010).

**Spectrum of inflammatory response**

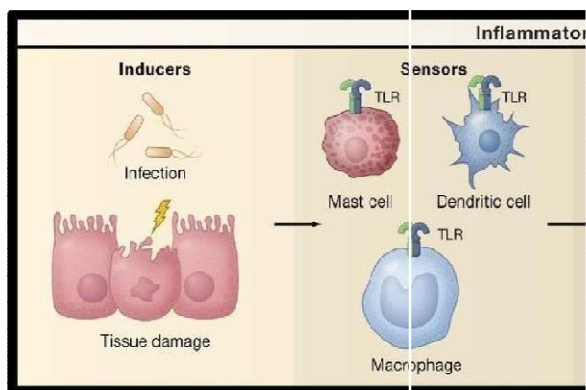


Fig: 1.1 Inflammatory pathway components

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