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Review

The role of serratiopeptidase in the resolution of inflammation

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ABSTRACT

Inflammation remains a key event during most of the diseases and physiological imbalance. Acute inflammation is an essential physiological event by immune system for a protective measure to remove cause of inflammation and failure of resolution lead to chronic inflammation. Over a period of time, a number of drugs mostly chemical have been deployed to combat acute and chronic inflammation. Recently, enzyme based anti-inflammatory drugs became popular over conventional chemical based drugs. Serratiopeptidase, a proteolytic enzyme from trypsin family, possesses tremendous scope in combating inflammation. Serine protease possesses a higher affinity for cyclooxygenase (COX-I and COX-II), a key enzyme associated with production of different inflammatory mediators including interleukins (IL), prostaglandins (PGs) and thromboxane (TXs) etc. Currently, arthritis, sinusitis, bronchitis, fibrocystic breast disease, and carpal tunnel syndrome, etc. are the leading inflammatory disorders that affected the entire the globe. In order to conquer inflammation, both acute and chronic world, physician mostly relies on conventional drugs. The most common drugs to combat acute inflammation are Nonsteroidal anti-inflammatory drugs (NSAIDs) alone and or in combination with other drugs. However, during chronic inflammation, NSAIDs are often used with steroidal drugs such as autoimmune disorders. These drugs possess several limitations such as side effects, ADR, etc. In order to overcome these limitations and complications, enzyme based drugs (anti-inflammatory) emerged, and aim for a new high since the last decade. Serine protease, the largest proteolytic family has been reported for several therapeutic applications, including anti-inflammatory. Serratiopeptidase is a leading enzyme which has a very long history in medical as an effective anti-inflammatory drug. Current study emphasizes present scenario and future prospect of serratiopeptidase as an anti-inflammatory drug. The study also illustrates a comparative analysis of conventional drugs and enzyme based therapeutic to combat inflammation.

Abbreviations: COX, cyclooxygenase; t-PA, tissue plasminogen activator; NSAIDs, non-steroidal anti-inflammatory drugs; ALL, acute lymphoblastic leukemia; ADR, adverse drug reaction; EC, enzyme commission; IL, interleukins; PGs, prostaglandins; TXs, thromboxane; LOX, lipoxygenase; RA, rheumatoid arthritis; SPMs, specialized pro-resolvins mediators.

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1. Overview

The enzyme-based therapeutics became an integral part of modern medicine mainly due to their selectivity and efficiency [1,2]. In general, the enzymes are basically proteins that possess the tremendous catalytic capacity and offer robust implications in modern healthcare [3,4]. Inflammation is a physiological response (immune response) against infection, injuries, autoimmune disorders and several diseases. In order to maintain physiological homeostasis, acute inflammation is essential and requires complete resolution [5]. The resolution of inflammation defines tissues homeostasis and balanced immune activity. However, failure of self-resolution of acute inflammation results in chronic inflammation and remains a major challenge [6]. Enzymes were first used as an anti-inflammatory in modern medicine in the 1950s when it was discovered in the United States that intravenous trypsin could relieve inflammation caused by rheumatoid arthritis, ulcerative colitis, and atypical viral pneumonia as well as post-surgical swelling and bruises caused by sports injuries [7,8]. As per reports published, Japanese began using serratiopeptidase for inflammation in 1957. The increasing success of enzyme therapeutics leads to the application of empirically encapsulated enzyme, including trypsin, chymotrypsin, and bromelain via oral administration [6]. Over the 1980s and early 1990s, Japanese and European researchers compared several enzymes for potential anti-inflammatory activity, and their study indicated that serratiopeptidase was the most effective of all of them in reducing the inflammation response [9]. Currently, serratiopeptidase became widely used in Japan and Europe as the anti-inflammatory and pain treatment of choice [10].

2. Mechanism of inflammation

Inflammation is a protective measure which evolved in advance animal to combat primarily injury and infection [11]. The immune system rapidly responds to any foreign and unwanted change in the tissues, leading to recruitment of immune cells and several other inflammatory mediators. In another word, inflammation is a cleaning process of invading elements and noxious changes leading to maintenance of homeostasis [12]. The acute and chronic inflammation is categorized based on the intensity of trigger and a pathological condition of the tissues. The molecular biology of inflammation is quite complex and associated with enormous numbers of player, including infectious agents, proteins, short peptides, enzyme, and hormones, etc [13]. The external signal is the core element for causing both acute and chronic inflammation later. More important, internal triggers became more devastating in the modern period. Autoimmune disorders such as rheumatoid arthritis (RA) are much more difficult for treatment as our internal biomolecule start acting as a trigger for the immune system [14]. The inflammation lead to several life-threatening diseases and disorders became a major hallmark [15,16]. However, the pathogenesis, i.e., both the cause and effect of inflammatory diseases, is difficult to pinpoint [17].

Modern research findings have revealed that inflammation plays a critical role in promoting cancer, in particular, the tumourigenesis, and a process of tumor formation [18,19] (Fig. 1). In addition to cancer cells, various types of immune cells are commonly found in tumors. Inflammation, both acute and chronic, leads to the production of physiologically active biomolecules like interleukins, cytokines and other short peptides like kallikreins associated with the fine tuning of the immune

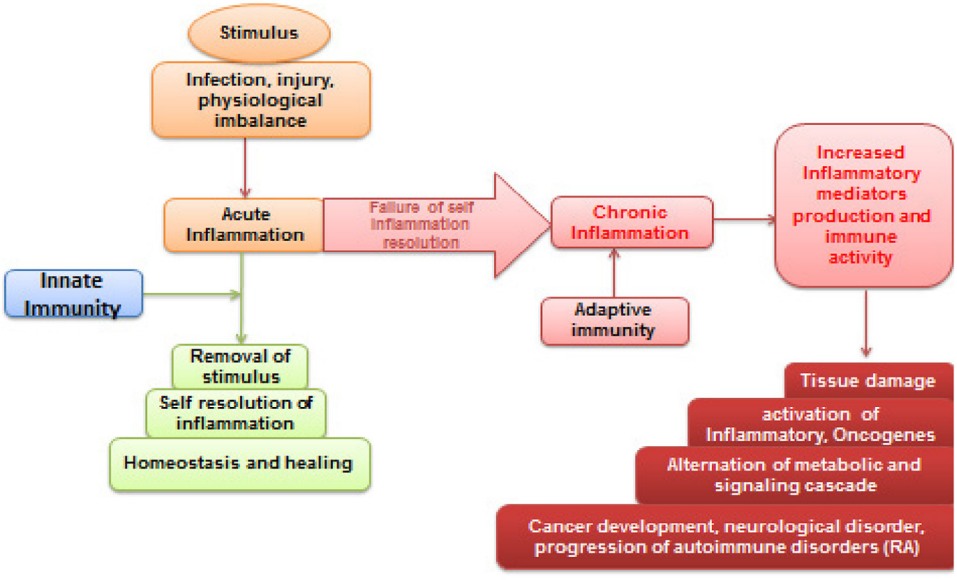

Fig. 1 – A detailed overview of various causes resulting in inflammation. Both environmental and endogenous factors are equally associated with the generation of inflammatory mediators and these mediators further affect tissues of normal homeostasis by affecting blood and lymph flow.