EFFECT OF BOSWELLIC ACIDS ON COMPLEMENT IN ADJUVANT- AND CARRAGEENAN-INDUCED INFLAMMATION

A. KAPIL
Pharmacology Division, Regional Research Laboratory, Jammu Tawi-180 001, India

ABSTRACT

The in-vivo effects of non-steroidal anti-inflammatory agents on the host immune system are still poorly understood. However, through inhibition of complement, boswellic acids (BA) exhibit adjuvant-induced and carrageenan-induced anti-inflammatory properties. The present work was aimed at evaluating the influence of BA on complement-related inflammation in the experimental models of inflammation. In adjuvant-induced arthritis and carrageenan-induced paw oedema in rats, BA were found to possess significant anti-inflammatory and complement-inhibitory activities. The intraperitoneal injection of BA (100 mg/kg twice a day), before and after FCA challenge and thereafter repeated for several days, significantly reduced foot pad thickness of experimental animal models and simultaneously also reduced complement activity. It also showed marked reduction in complement levels and inflammatory effects on carrageenan-induced paw oedema in rats when injected intraperitoneally (100 mg/kg twice a day).

Keywords: Boswellic acids, inflammation, complement

INTRODUCTION
Boswellic acids, a mixture of four pentacyclic triterpene acids, an alcoholic extract of salai guggal, the oleo gum resin obtained from Boswellia serrata, has been reported to possess marked anti-inflammatory and anti-arthritic activities [1,2]. Complement system has been shown to influence each of the factors that comprise the inflammatory response through release of anaphylatoxins [3]. In addition to the direct effects of anaphylatoxins, complement activation products elicit the synthesis and/or secretion of numerous other inflammatory mediators, e.g. synthesis and secretion of the proinflammatory cytokine, IL-1, by macrophages [4], by stimulating the platelet release reaction followed by aggregation [5], and by generating prostaglandins from macrophages [6,7]. Insertion of the membrane attack complex (C5b-9) in sublytic amounts into the membrane of nucleated cells and platelets also stimulates arachidonate metabolism and can cause release of prostaglandin E2, leukotriene B4 and thromboxane, the secondary mediators that are postulated to contribute to inflammation induced by complement activation in tissues [8].

It has also been observed that complement-induced alteration in the cell surface as well as the interactions of receptors, including complement receptors, in adherence to the vascular endothelium clearly enhances inflammation [8]. The pro-inflammatory role of complement activation in experimental models has been demonstrated [9] and the research on anti-inflammatory tests with Freund's adjuvant polyarthritis of rats being the only immunological model in current use [10]. A strong correlation between
complement inhibitory and anti-inflammatory activity in experimental models has been observed [11,12].

It is also well established that serum complement is activated by carrageenan and levels of activated complement are increased throughout the first six hours of the inflammatory response towards carrageenan [13].

Boswellic acids, a selective inhibitor of C3-convertase of classical complement pathway [14], is tested for its effect on complement and inflammatory activities in the experimental animal models.

MATERIALS AND METHODS

Animals

Well-fed and hygenically maintained male albino Charles Foster rats (80–90 g) were obtained from our laboratory animal house.

Arthritis induced by Freund's complete adjuvant

For arthritis, a total of 15 rats divided into three groups, each containing 5 rats, were innoculated with Freund's complete adjuvant (FCA, Sigma Co.). Each rat received a subplantar injection of 250 µl of FCA in the midline–midmetatarsal region of the left hind foot pad. Boswellic acids (obtained from the Natural Product Chemistry division of the laboratory) and the standard anti-inflammatory drug, ibuprofen (Boots, Bombay, India), 100 mg/0.2 ml normal saline per kg were injected intraperitoneally twice daily for five days respectively 1 h before adjuvant challenge to the two groups of rats, and the remaining group of five rats received an equivalent volume of saline and served as a control. This dose corresponded to the approximate ED30 for anti-oedemic activity.

Carrageenan-induced paw oedema in rats

Acute paw oedema in rats was induced by injecting 0.1 ml of 1% (w/v) sterile carrageenan prepared in normal saline (Marine Colloids Div., Springfield, USA) into the subplantar region of the left hind paw [15]. The test samples, boswellic acids* and standard anti-inflammatory drug, ibuprofen, were injected intraperitoneally (100 mg/0.2 ml normal saline per kg) into the two groups of rats respectively twice a day, 30 min before and 3 h after carrageenan challenge. One of the third group of rats received normal saline and served as a control.

*The chemical composition of the material is as follows:

- β-boswellic acid (50 ± 2%)
- 3-acetyl-β-boswellic acid (30 ± 2%)
- 11-keto-β-boswellic acid (7 ± 1%)
- 3-acetyl-11-keto-β-boswellic acid (7 ± 1%)