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Review

Marine algae as a potential pharmaceutical source for anti-allergic therapeutics

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ABSTRACT

The prevalence of allergic diseases such as asthma, atopic dermatitis, and allergic rhinitis has increased during the last two decades and contributed a great deal to morbidity and an appreciable mortality in the world. Until now, few novel efficacious drugs have been discovered to treat, control or even cure these diseases with a low adverse-effect profile. Meanwhile, glucocorticoids are still the mainstay for the treatment of allergic disease. Therefore, it is necessary to isolate novel anti-allergic agents from natural resources. Recently, marine algae have received much attention as they are a valuable source of chemically diverse bioactive compounds with numerous health benefit effects. This review focuses on anti-allergic agents derived from marine algae and presents an overview of their pharmaceutical potential in the treatment of allergic disorders.

Contents

1. Introduction

Allergic diseases are one of the major public health problems in the developed world. It was estimated that approximately one-third of the general population and one-fifth of the population in western countries were affected by allergic diseases [1,2]. Specially, allergic rhinitis, asthma, and atopic eczema are among the commonest causes of chronic ill-health. The prevalence, severity, and complexity of these allergic diseases are rapidly rising and considerably adding to the burden of health-care costs [3]. Therefore, the knowledge about the pathophysiology of allergic diseases has increased, offering new opportunities for therapeutic intervention. Substantially, allergy is caused by an exaggerated reaction of the immune system to harmless environmental substances, such as animal dander, house dust mites, foods, pollen, insects, and

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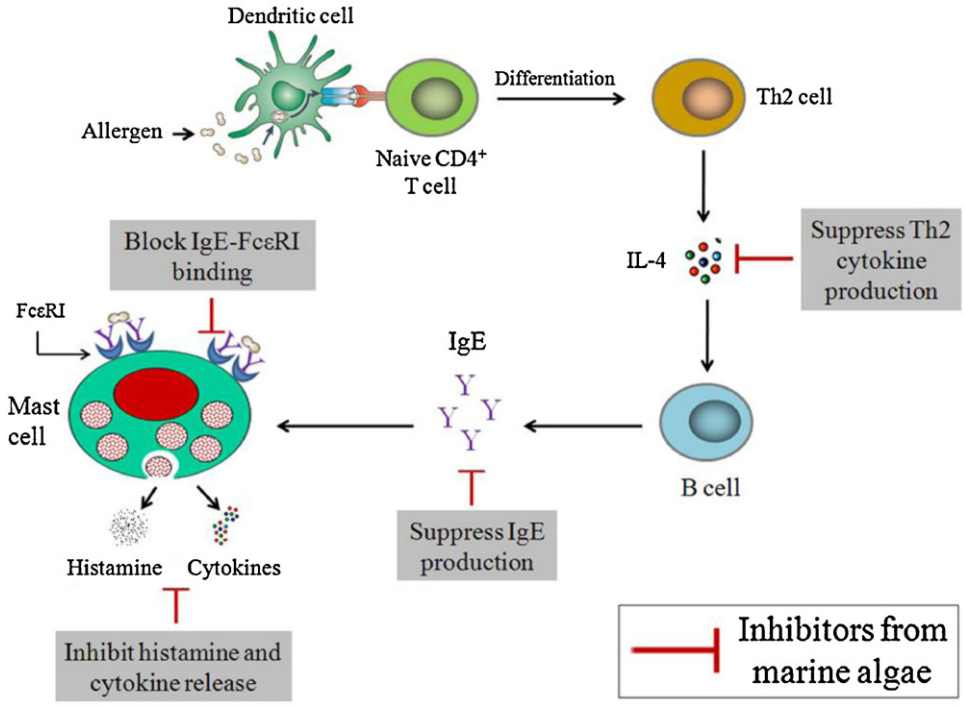

Fig. 1. Potential targets for *therapeutic intervention* in *allergy*.

chemical agents [4,5]. The initial event responsible for the development of allergic diseases is the generation of allergen-specific $CD4^+$ Th2 cells. Once generated, effector Th2 cells produce IL-4, IL-5, IL-9, and IL-13 which cause the production of allergen-specific IgE by B cells [6]. Subsequently, allergic reactions are induced upon binding of allergen to IgE, which is tethered to the high affinity IgE receptor on the surface of mast cells and basophils. Following the aggregation of cell-surface receptors is a cascade of intracellular events, including the increase of intracellular Ca^{2+} level, the release of preformed inflammatory mediators from secretory granules such as histamine and β-hexosaminidase, the generation and secretion of the newly synthesized substances such as leukotrienes, prostaglandins, and cytokines. These mediators cause allergic inflammatory responses due to airway constriction, mucous production, and recruitment of inflammatory cells [7,8]. According to this mechanism, the control of Th2-type cytokine expression, IgE levels, and inflammatory mediator production are especially important for the regulation of type I allergic reaction, thus allergic diseases may be managed (Fig. 1). The current drugs that are used to treat allergies, such as antihistamines or corticosteroids, ameliorate symptoms but do not stop progression [9]. There are also concerns regarding the side-effects from chronic use of current drugs, particularly by children [10]. Thus, the search for potential drug candidates containing higher anti-allergy activity is increasing in the pharmaceutical industry. In this regard, natural bioactive compounds and their derivatives are great sources for the development of new generation anti-allergic therapeutics which are more effective with fewer side-effects.

The world's oceans, covering more than 70% of the earth's surface, represent an enormous resource for the discovery of potential therapeutic agents. During the last decades, numerous novel compounds have been isolated from marine organisms and many of these substances have interesting biological activities [11–14]. Notably, marine algae are known to be one of the most important producers of biomass in the marine environment. They produce a wide variety of chemically active metabolites in their surroundings as an aid to protect themselves against other settling organisms [15]. Interestingly, marine algae have been revealed to possess anti-coagulant, anti-viral, anti-oxidant, anti-allergic, anti-cancer, anti-inflammatory, and anti-obesity activities [16–20]. Therefore, marine algae are believed to be a promising source to provide not only novel biologically active substances for the development of pharmaceuticals but also essential compounds for human nutrition [16,21]. So far, brown algal *Sargassum hemiphyllum* and red algal *Carpopeltis affinis* have been used in Korean folk medicine as a therapeutic treatment of various allergic diseases [22,23]. Recently, the role of marine algae as anti-allergic agents has been determined *in vitro* and *in vivo* by many researchers. Simultaneously, numerous marine algae have been found to be efficient for anti-allergic therapeutics. This review, therefore, focuses specifically on the anti-allergic effects of marine algae and emphasizes their potential application as candidates of pharmaceuticals as well as nutraceuticals to prevent allergic disorders.

2. Marine algae with their anti-allergic activities

2.1. Brown macroalgae

Although marine algae were believed to be safe and efficient agents for anti-allergic treatment, they have not been as extensively studied as terrestrial plants. Recently, a number of brown macroalgae have been determined for their capability against allergic responses (Table 1). According to Kimiya et al. [24], various extracts of *Ecklonia cava*, *Chrysymenia wrightii*, *Petalonia binghamiae*, *Scytosiphon lomentaria*, *Undaria pinnatifida*, *Porphyra dentata*, *Codium fragile*, and *Ulva japonica* have been found to inhibit more than 50% of β-hexosaminidase release from RBL-2H3 cells at concentrations of 100 and 200 μg/ml. Among them, *P. binghamiae* appeared to be most effective against degranulation of both RBL-2H3 cells and mouse eosinophils. Likewise, the anti-allergic property of forty-one marine macroalgae collected from the Ise-Shima region of Mie Prefecture, Japan was elucidated by Sugiura et al. [25].