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4-((E)-3-(4-(octyloxy)phenyl)acryloyl)phenylboronic Acid: Synthesis and Health Benefits

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Abstract - When it comes to protecting the body from harmful substances, the immune system is first line of defence. Lymph nodes, tonsils, adenoids, and the thymus are only few of the organs and tissues that make up the human immune system. Germs need to get past the body's natural defences, such mucus and enzymes, before they can infect a host. In order to begin destroying healthy cells, they must first overcome these barriers. If a pathogen is able to get past the first layer of defence, it will be sent to the next level of protection. There are two main types of immune system responses to infections: innate and adaptive. Host innate or nonspecific immune cells like macrophages and dendritic cells are responsible for the early response to infections. Specific immunity, or acquired immunity, is established by the body's manufacture of antibodies that are highly specific to the antigens that caused an infection. Both naturally occurring chalcones and synthetically synthesised chalcones, together with their respective derivatives, have been shown to possess intrinsic anticancer and anti-inflammatory effects. Clinical trials are currently the only reliable means of gauging a treatment's potential therapeutic benefit. In order to create more effective molecules, it would be helpful to have access to compounds with well-defined mechanisms of action. In this research, we synthesised a boronic Chalcone derivative and analysed its immunomodulatory effects.

Keywords - Chalcones,Immunity, NMR, Boronicchalcones, Immunomodulatory agents

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INTRODUCTION

The immune system is the principal defensive mechanism for all living creatures, acting as a protective barrier against pathogens that might be harmful to the body. The thymus, tonsils, adenoids, spleen, and lymph nodes are all parts of the human immune system. The human immune system is made up of several different organs and tissues. In order for pathogens to cause an infection, they need to be able to break through physiological barriers such as mucus and enzymes, and they also need to be able to have a detrimental impact on live cells. In the event that a pathogen is successful in penetrating the first line of protection, it will then trigger the activation of the secondary line of defence. The immune system has the ability to produce one of two distinct reactions whenever it is confronted with an invasive infection. Innate immunity, which also goes by the name nonspecific immunity, is the main defensive mechanism that is activated in the immunological response of a host when it encounters an infection. Phagocytes, more particularly macrophages and dendritic cells, are found inside the immune system and serve as the major defence mechanism. Acquired immunity, also known as specific immunity, gets rid of pathogens in the latter stages of an infection and creates immunological memory by producing antibodies that target antigens in a particular way. The term "specific immunity" is often used to refer to this kind of immunity. Different clinical issues have been shown to have an association with anomalies in the development or function of immune cells. This correlation has been identified. These worries involve conditions such as atherosclerosis and autoimmune diseases as well as TB. According to the results of the study that was conducted, it has been seen that persons who have been diagnosed with a severe form of tuberculosis (TB) have lower numbers of CD4+ and CD8+ T cells. This suggests that the individual's immune system may not be functioning as well as it once did. Because of the production of a heat-labile component that is toxic to T cells, it is believed that macrophages that have been infected with Mycobacterium TB are involved in the pathogenesis of tuberculosis. It is not uncommon for people who have been diagnosed with tuberculosis (TB) to have impaired immune systems. Monocytes that are circulating in the bloodstream bind to damaged endothelium that is found in the tunica intima. The subsequent adherence of these monocytes results in the release of cytokines and

mediators, which in turn leads to the synthesis of related proteins. The intima is the anatomical area that monocytes change into macrophages via the process of differentiation. This process takes place in this part of the vascular wall. As atherosclerosis progresses, macrophages take in oxidised low-density lipoprotein via scavenger receptors, which causes the subsequent release of foam cells into the circulation. This is one step in the progression of atherosclerosis. The foam cells play an essential role in the process as a whole. Interferon, glatiramer acetate, and mitoxantrone are only three of the immunomodulatory drugs that have undergone extensive testing as potential treatments for multiple sclerosis (MS). It is possible to treat autoimmune conditions, such as systemic lupus erythematosus, multiple sclerosis, and myasthenia gravis, using intravenous immunoglobulin treatment. Chalcones, also known as 1,3-diaryl-2-propen-1-ones, may be found in a wide variety of edible plants. These compounds serve as the precursors for flavonoids and isoflavonoids, as seen in Figure 1. The chalcone derivatives provide a wide variety of pharmacological advantages, including the ability to effectively treat HIV, cancer, malaria, and bacterial infections, amongst other conditions. Furthermore, chalcone molecules have been shown to possess anti-inflammatory activities, which have been supported by empirical studies (8-13). It has been discovered that chalcone derivatives have the capacity to impede neutrophil chemotaxis and phagocytosis. These observations are based on the results of two experiments that were conducted independently of one another. In addition to this, it has been shown that these compounds are capable of inhibiting the production of proinflammatory cytokines, lipoxygenases, COX, reactive oxygen species, and lipoperoxidation (ROS). The coordinates that have been supplied are (14,15). In recent years, a substantial amount of research has been carried out to investigate the pharmacological activities and signalling mechanisms associated with chalcone derivatives. The persons whose ages are being considered fall somewhere in the range of 16 to 18 years old. The knowledge that is currently accessible, however, is insufficient in reference to the impact that chalcone derivatives have on the many different kinds of immune cells. This article provides a comprehensive examination of the activity shown by a variety of chalcone derivatives across a broad spectrum of immune cell types. The major goal is to make progress in the creation of therapeutic drugs that are capable of effectively targeting and treating pathological illnesses that are associated to immunological disorders.

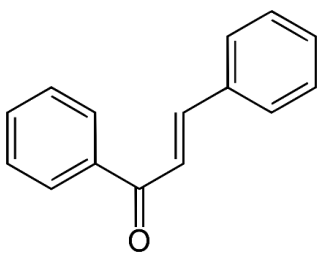

Figure 1: Basic structure

MATERIALS AND METHODS

Synthesis

In a 100-milliliter round-bottomed flask, 4-acetylphenylboronic acid was dissolved in ethanol. Ethanol and the acid were roughly at the same molarity level (approximately 20 mL each). Subsequently, 10% NaOH was added, and the reaction mixture was continuously stirred for 30 minutes at room temperature, equating to a five-fold excess of NaOH. After 18 hours of stirring, light yellow precipitates formed upon adding 1,000 grams of 4-alkoxybenzaldehyde A-F. The combination of ingredients preceded this step. To prevent further reactions, the process was halted by introducing 35 mL of crushed ice into the solid mass, followed by the addition of diluted hydrochloric acid. Components A through F were obtained in the form of yellow solids after filtering and recrystallizing the ethanol. These elements are listed alphabetically [19].

4-((E)-3-(4-(octyloxy)phenyl)acryloyl)phenylboronic acid (Compound B); The usual process was followed when 4-(octyloxy)benzaldehyde (0.998 g, 4.27 mmol) and acetylphenylboronic acid (0.710 g, 4.27 mmol) were reacted. The products were gathered as Solid beige.

^{1}H NMR: δ 0.86 (3H, t, *J* = 7.0 Hz), 1.17-1.44 (10H, 1.23 (quint, *J* = 7.0 Hz), 1.24 (quint, *J* = 7.0 Hz), 1.28 (h, *J* = 7.0 Hz), 1.28 (quint, *J* = 7.0 Hz), 1.38 (tt, *J* = 7.5, 7.0 Hz)), 1.82 (2H, quint, *J* = 7.5 Hz), 4.23 (2H, t, *J* = 7.4 Hz), 6.68 (1H, d, *J* = 15.6 Hz), 7.19 (2H, ddd, *J* = 8.8, 1.0, 0.5 Hz), 7.43-7.68 (5H, 7.50 (ddd, *J* = 8.8, 1.7, 0.5 Hz), 7.53 (ddd, *J* = 7.8, 1.4, 0.5 Hz), 7.61 (d, *J* = 15.6 Hz)), 7.77 (2H, ddd, *J* = 7.8, 1.7, 0.5 Hz)

^{13}C NMR: δ 14.0 (1C, s), 22.6 (1C, s), 25.8 (1C, s), 29.3 (1C, s), 29.3-29.4 (2C, 29.4 (s), 29.4 (s)), 31.8 (1C, s), 69.1 (1C, s), 114.3 (2C, s), 121.2 (1C, s), 127.8 (2C, s), 128.7 (2C, s), 130.3 (1C, s), 133.6 (1C, s), 135.0 (2C, s), 135.5 (1C, s), 144.1 (1C, s), 158.5 (1C, s), 188.9 (1C, s)

m/z: 380.22 (100.0%), 381.22 (24.1%), 379.22 (23.4%), 382.22 (3.6%)

Immunomodulatory activity

In this study, we employed the J774A.1 mouse macrophage cell line sourced from the American Type Culture Collection (ATCC). Cultivation was carried out using RPMI 1640 complete growth media (Sigma). The media used, Gibco's IMDM, which is manufactured in the United States, contained 1% neomycin, 1% streptomycin, 1% penicillin, and 12% fetal bovine serum. Macrophage viability was assessed using trypan blue staining (Gibco) following a standard protocol.

RESULTS AND DISCUSSION

4-((E)-3-(4-(octyloxy)phenyl)acryloyl)phenylboronic acidgeneral properties of the (compound X)

Drug discovery and development is a resource-intensive and time-consuming endeavor. It involves the exploration of diverse molecular structures across a broad spectrum of parameters to influence

the selection of compounds for synthesis, testing, and eventual promotion. In this study, we employed ChemDraw to generate 2D (Figure 2) and 3D (Figure 3) molecular structures before proceeding with synthesis. The key attributes of the synthesized Compound X are outlined in Table 1.

Table 1: General properties of Compound X

Compound	Colour	% Yield	M.P.
Compound X	55%	Beige Solids	102±4 °C

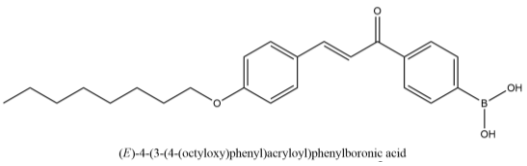

Figure 2: Synthesised molecule structure

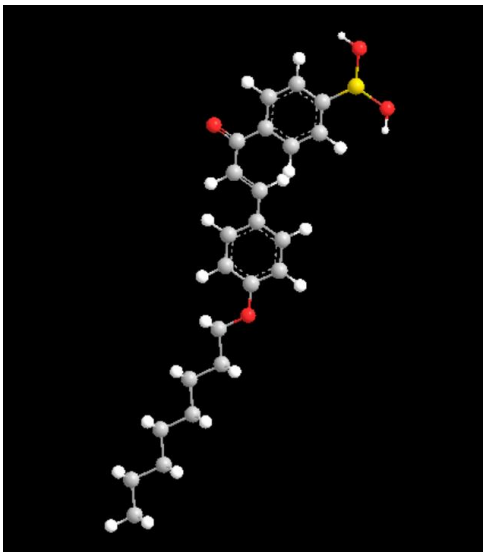

Figure 3: 3D structure of the synthesised molecule

Immunomodulatory effects of Compound X

The human body is equipped with a highly effective defence mechanism, which consists of both the innate and adaptive immune systems. The innate immune system exhibits prompt responsiveness, offering defence within a few hours of pathogen exposure, independent of the presence of particular antigens. Nevertheless, it exhibits a deficiency in generating enduring immunological memory, thereby impeding the body's ability to identify the identical pathogen during subsequent encounters. The concept of innate immunity involves four main defence mechanisms: endocytosis and phagocytosis, inflammation, physiological barriers (including temperature, low pH, and chemical mediators), and physical barriers (such as the skin and mucous membranes).

Phagocytic cells, such as neutrophils, monocytes, and macrophages, play a crucial role in the innate immune response. In addition to the aforementioned immune cells, namely NK cells, basophils, mast cells, and eosinophils, these cells also actively contribute to the functioning of the defence system. Phagocytosis encompasses several essential stages, which include the activation of actin polymerization in response to signals from pathogen-receptor complexes, the identification and attachment of pathogens to receptors on the cell surface, and the creation of membrane extensions rich in actin that engulf and transport the pathogen towards the centre of the cell. Phagocytosis can only occur when cell surface receptors recognise and bind to specific pathogens. Following this, a phagolysosome is generated, which is equipped with hydrolytic and acidic enzymes, with the purpose of eradicating the infection.

The innate immune system relies on various molecular components, such as complement, acute-phase proteins, and cytokines. Soluble mediators, such as cytokines, play a crucial role in facilitating the recruitment of immune cells to sites of infection. The mediators described here have the ability to augment antibody production, initiate the complement system, and enhance opsonization, thereby increasing the efficiency of phagocytosis. Acute-phase proteins, such as C-reactive protein, play a crucial role in facilitating tissue repair and enhancing the immune system.

Antigen-presenting cells (APCs) are a specialised cell type that plays a pivotal role in the initiation of adaptive immune responses. Their primary function is to present antigens that are recognised by the innate immune system. [20-27]

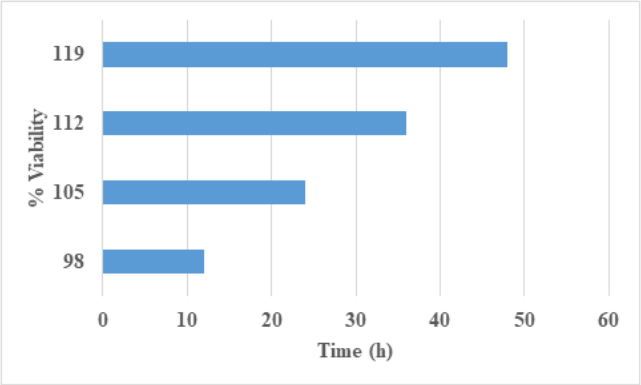

Figure 4: Effects of the compound X on the macrophage viability for verifying its immunomodulatory potential.

CONCLUSION

In summary, this study demonstrates the successful synthesis of Compound X with a high yield. The experimental model employed reveals that Compound X exhibits notable immunomodulatory effects. Consequently, our research provides a

valuable foundation for future investigations in drug development and discovery, potentially leading to the creation of additional bioactive Chalcone derivatives.

AUTHOR CONTRIBUTION

Equal contribution by all authors

CONFLICT OF INTEREST

None to declare

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