Journal of Advances and Scholarly Researches in Allied Education
Vol. 20, Issue No. 1, January-2023, ISSN 2230-7540

Synthesis, Characterization and Immunomodulatory Effects of 4-((E)-3-(4-heptyloxy)phenyl acryloyl} phenyloboronic Acid

Manjit Singh[1], Vikrant Jain[2]*

[1,2] Department of Chemistry, Madhyanchal Professional University, Bhopal 462044, India

*Email:dr_vikrantjain@yahoo.co.in

Abstract - The immune system is the body's main line of defence against pathogens. The human immune system is comprised of several different organs and tissues, including lymph nodes, tonsils, adenoids, and the thymus. In order to infect a host, germs must first overcome physical barriers like mucus and enzymes before they can begin destroying healthy cells. If a pathogen gets beyond the first line of defence, it will be sent to the second line. There are two main categories of immune responses to infections: innate and adaptive. Host defence against infections begins with phagocytes like macrophages and dendritic cells, which are part of the host's innate or nonspecific immunity. Acquired immunity, also known as particular immunity, removes pathogens in the late stages of infection and generates immunological memory by means of the formation of antigen-specific antibodies.It has been shown that naturally occurring chalcones as well as synthetically produced chalcones and their derivatives have anticancer and anti-inflammatory properties. Clinical testing is the only reliable method for determining their potential therapeutic benefit. Compounds that possess well-understood mechanisms of action have the potential to be used as fundamental building blocks in the production of further molecules that are much more efficient. In this study we synthesized the boronic Chalcone derivative and evaluated its immunomodulatory potential.

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

----------X----------

INTRODUCTION

The immune system is the first line of defence for all living organisms, acting as a barrier between them and harmful infections. A small selection of the organs and tissues that come together to form the human immune system include the thymus, tonsils, adenoids, spleen, and lymph nodes. If pathogens are going to cause an infection, they need to be able to break through physiological barriers like mucus and enzymes, and they also need to have a negative effect on living cells. If a pathogen is able to breach the first layer of defence, it will be transferred to the second line of defence. There are two possible ways in which the immune system will respond when it is faced with an invasive infection. Innate immunity, often referred to as nonspecific immunity, is the first line of defence in the host's defence against infections. This immunity is comprised of phagocytes such as macrophages and dendritic cells as the first line of defence. Acquired immunity, sometimes referred to as particular immunity, eliminates pathogens in the latter stages of an infection and establishes immunological memory via the development of antigen-specific antibodies. This kind of immunity is also known as particular immunity. (1) There is a correlation between abnormalities in the formation or function of immune cells and a broad variety of clinical concerns, such as autoimmune disease, tuberculosis, and atherosclerosis. (2,3) Those with severe TB have been shown to have less CD4+ and CD8+ T cells, which may be an indication of a weakened immune system. Macrophages that have been infected with Mycobacterium tuberculosis are thought to be responsible for the pathogenesis of tuberculosis by secreting a heat-labile factor that is cytotoxic to T cells. TB sufferers' immune systems are impaired. (4) Circulating monocytes create cytokines and mediators by sticking to injured endothelium in the tunica intima and secreting the associated proteins. The intima is where monocytes undergo the process of differentiation into macrophages. In the process of developing atherosclerosis, macrophages take in oxidised low-density lipoprotein via the use of scavenger receptors and subsequently release foam cells into the circulation. These foam cells are an essential component of the process. (5) A number of immunomodulatory medications, including interferon, glatiramer acetate, and mitoxantrone, have been tried and tested in the treatment of multiple sclerosis (6). An alternate approach to treating autoimmune diseases such systemic lupus erythematosus, multiple sclerosis, and myasthenia gravis is the use of intravenous immunoglobulin. (7) There are many

www.ignited.in

different types of food plants that contain chalcones (1,3-diaryl-2-propen-1-ones), which are the precursors of flavonoids and isoflavonoids (Figure 1). The anti-HIV, anti-cancer, anti-malarial, and antibacterial effects of chalcone derivatives are only some of the many pharmacological advantages of these compounds. In addition, it has been shown that chalcone molecules have anti-inflammatory properties. (8–13) According to the findings of two separate studies, chalcone derivatives have the ability to prevent neutrophil chemotaxis and phagocytosis, as well as the production of proinflammatory cytokines, lipoxygenases, COX, reactive oxygen species, and lipoperoxidation (ROS). (14,15) The pharmacological actions and signalling pathways that are mediated by chalcone derivatives have been the subject of a significant amount of study in recent years. (16–18) Regrettably, there is a lack of information on the manner in which chalcone derivatives influence the various immune cell types. This article covers in full the activity of several chalcone derivatives in various immune cells with the intention of one day developing therapeutic drugs to combat pathological conditions related with immune illnesses.

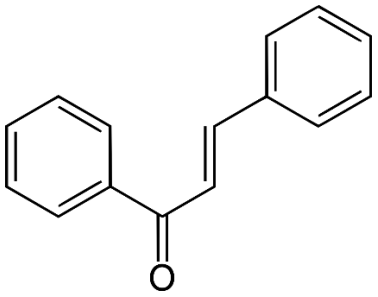


Figure 1: Basic structure

MATERIALS AND METHODS

Synthesis

In a round-bottomed, one hundred millilitre flask, 4-acetylphenylboronic acid was dissolved in ethanol. In terms of molarity, ethanol and acid were about on par (20 mL). After adding 10% NaOH, the reaction mixture was agitated continuously for 30 minutes at room temperature (five equivalent). Light yellow precipitates appeared after 18 hours of stirring and the addition of 1,000 grammes of 4-alkoxybenzaldehyde A-F. This happened after the ingredients had been combined first. The process was stopped when 35 mL of broken ice was injected into the solid mass together with diluted hydrochloric acid. This was done to forestall any additional reactions. Components A through F, in the form of yellow solids, were obtained after the ethanol had been filtered and recrystallized. This set of elements is presented in alphabetical order. [19]

4-((E)-3-(4-heptyloxy)phenyl)acryloyl)phenyloboronic acid: Typically, 4-(heptyloxy)benzaldehyde (1.007 g, 4.54 mmol) was mixed with acetylphenylboronic acid (0.755 g, 4.54 mmol) using the standard procedure. The products were gathered with the help of Yellow Solids.

^{1}H NMR: δ 0.86 (3H, t, *J* = 7.0 Hz), 1.18-1.44 (8H, 1.24 (quint, *J* = 7.0 Hz), 1.28 (quint, *J* = 7.0 Hz), 1.28 (h, *J* = 7.0 Hz), 1.37 (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), 29.4 (1C, 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)

Immunomodulatory activity

The current investigation takes use of the American Type Culture Collection's J774A.1 mouse macrophage cell line (ATCC). Complete growth media RPMI 1640 was used for cultivation (Sigma). Made in the USA, Gibco's IMDM includes 1% each of neomycin, streptomycin, and penicillin in addition to 12% foetal bovine serum. The macrophage viability was determined by trypan blue staining (Gibco) by following standard protocol.

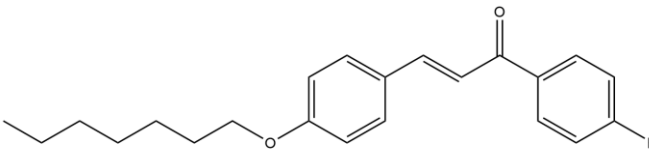
Results and Discussion

4-((E)-3-(4-heptyloxy)phenyl)acryloyl)phenyloboronic acid general properties of the (compound A)

In order to impact the selection of compounds for synthesis, testing, and promotion, drug discovery and development is a time-consuming and costly process that requires examining a wide variety of molecular structures based on a wide variety of parameters. Herein, we used chemdraw for formation of 2D (Figure 2) and 3D structure creation (Figure 3) and then synthesis was performed. The general characteristics of the synthesized compound are shown in table 1.

Table 1: General properties of compound A

Compound	Colour	% Yield	M.P.
Compound A	Yellow Solids	75%	100±4 °C



(*E*)-4-(3-(4-(heptyloxy)phenyl)acryloyl)phenylboronic acid

\

Figure 2: Synthesised molecule structure

www.ignited.in

Figure 3: 3D structure of the synthesised molecule

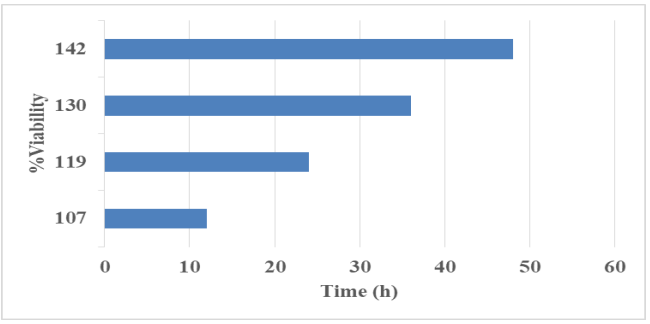


Figure 4: Effects of the compound A on the macrophage viability for verifying its immunomodulatory potential.

Immunomodulatory effects of compound A

Since it has both an innate and an adaptive immune system, the human body is equipped with a comprehensive defence mechanism. The host is protected either instantaneously or within hours of being exposed to a disease by a defence mechanism called innate immunity, which does not need the presence of an antigen. Memory cannot be stored in the immune system. Because of this kind of immunity, the body will not be able to recognise the same illness in the future. As a result. Innate immunity is comprised of four primary defence mechanisms: endocytosis and phagocytosis, inflammation, physiological barriers (temperature, low pH, and chemical mediators), and physical barriers (skin and mucous membranes). Innate immunity also includes phagocytic cells such as neutrophils, monocytes, and macrophages, all of which play essential roles in the immune response. NK cells, basophils, mast cells, and eosinophils are all involved in the immune response. Actin polymerization subcellularly in response to signals from the pathogen-receptor complex, pathogen identification and binding to cell surface receptors, and actin-rich membrane extension that envelops and drags the pathogen towards the cell centre are all crucial steps in the phagocytosis process. Cells can only phagocytose pathogens that have been recognised and bound to cell surface receptors. After then, a phagolysosome that is equipped with hydrolytic and acidic enzymes is produced and given the responsibility of eliminating the infection. Complement, acute-phase proteins, and cytokines are examples of the kinds of molecular components that are essential to the operation of innate immune processes. With the action of cytokines, which belong to the family of soluble mediators, innate immunity is responsible for bringing immune cells to the sites of infections. Because of these mediators, antibody production will be boosted, and the complement system will be activated; as a result, the target antigen will become more opsonized, and it will be simpler to phagocytose. The acute-phase proteins C-reactive protein and others like it help the body recover itself and enhance immunity. Antigen-presenting cells are a specialised cell type that, in response to antigens that are recognised by the body's innate immune system, have the potential to assist in the activation of an adaptive immune response. [20-27]

CONCLUSION

In conclusion, the results of this study revealed that we synthesised the compound A with high yield and the experimental model showed that compound A possesses remarkable immunomodulatory effects. Therefore, our study could be used for further studies to be carried out for drug development and discovery and result in the production of more bioactive Chalcone derivatives.

AUTHOR CONTRIBUTION

Equal contribution by all authors

CONFLICT OF INTEREST

None to declare

REFERENCES

1. Akira S, Uematsu S, Takeuchi O. Pathogen recognition and innate immunity. Cell. 2006;124(4):783–801.
2. Shalhoub J, Falck-Hansen MA, Davies AH, Monaco C. Innate immunity and monocyte-macrophage activation in atherosclerosis. J Inflamm (Lond). 2011;8:9.
3. Davoudi S, Rasoolinegad M, Younesian M, et al. CD4+ cell counts in patients with different clinical manifestations of tuberculosis. BrazJ Infect Dis. 2008;12(6):483–486.
4. Macdonald SH, Woodward E, Coleman MM, et al. Networked T cell death following macrophage infection by Mycobacterium tuberculosis. PLoS One. 2012;7(6):e38488.
5. Wilson HM. Macrophages heterogeneity in atherosclerosis – implications for therapy. J Cell Mol Med. 2010;14(8):2055–2065.
6. Kantarci OH, Pirko I, Rodriguez M. Novel immunomodulatory approaches for the management of multiple sclerosis. ClinPharmacolTher. 2014;95(1):32–44.
7. Arnson Y, Shoenfeld Y, Amital H. Intravenous immunoglobulin therapy for

autoimmune diseases. Autoimmunity. 2009;42(6):553–560.
8. Frölich S, Schubert C, Bienzle U, Jenett-Siems K. In vitro antiplasmodial activity of prenylatedchalcone derivatives of hops (Humuluslupulus) and their interaction with haemin. J AntimicrobChemother. 2005;55(6):883–887.
9. Abdula AM. Synthesis, characterization and antibacterial activity of (E)-chalcone derivatives. Eur J Chem. 2013;4(3):207–210.
10. Kim KN, Ko YJ, Kang MC, et al. Anti-inflammatory effects of trans-1,3-diphenyl-2,3-epoxypropane-1-one mediated by suppression of inflammatory mediators in LPS-stimulated RAW 264.7 macrophages. Food ChemToxicol. 2013;53:371–375.
11. Ku BM, Ryu HW, Lee YK, et al. 4′-Acetoamido-4-hydroxychalcone, a chalcone derivative, inhibits glioma growth and invasion through regulation of the tropomyosin 1 gene. BiochemBiophys Res Commun. 2010;402(3):525–530.
12. Rizvi SUF, Ahmad M, Bukhari MH, et al. Anti-HIV-1 screening of (2E)-3-(2-chloro-6-methyl/methoxyquinolin-3-yl)-1-(aryl)prop-2-en-1-ones. Med Chem Res. 2014;23(1):402–407.
13. Mohamad AS, Akhtar MN, Zakaria ZA, et al. Antinociceptive activity of a synthetic chalcone, flavokawin B on chemical and thermal models of nociception in mice. Eur J Pharmacol. 2010;647(1–3):103–109.
14. Bukhari SN, Lauro G, Jantan I, Bifulco G, Amjad MW. Pharmacological evaluation and docking studies of α,β-unsaturated carbonyl based synthetic compounds as inhibitors of secretory phospholipase A2, cyclooxygenases, lipoxygenase and proinflammatory cytokines. Bioorg Med Chem. 2014;22(15):4151–4161.
15. Bukhari SN, Tajuddin Y, Benedict VJ, et al. Synthesis and evaluation of chalcone derivatives as inhibitors of neutrophils' chemotaxis, phagocytosis and production of reactive oxygen species. ChemBiol Drug Des. 2014;83(2):198–206.
16. Alam MS. Biological potentials of chalcones: a review. Int J Pharm BiolSci Arch. 2012;3(6):1298–1303.
17. Rahman MA. Chalcone: a valuable insight into the recent advances and potential pharmacological activities. ChemSci J. 2011;2011(2):CSJ-29.
18. Yadav VR, Prasad S, Sung B, Aggarwal BB. The role of chalcones in suppression of NF-κB-mediated inflammation and cancer. IntImmunopharmacol. 2011;11(3):295–309.
19. McKoy DL. Synthesis And Characterization Of Boronic Acid Chalcones As Potential Cancer Chemoprevention Drug Candidates. 2013.
20. Warrington R, Watson W, Kim HL, Antonetti FR. An introduction to immunology and immunopathology. Allergy Asthma ClinImmunol. 2011;7Suppl 1:S1–S8.
21. Delves PJ, Roitt IM. The immune system. New Engl J Med. 2000;343(1):37–49.
22. Bonilla FA, Oettgen HC. Adaptive immunity. J Allergy ClinImmunol. 2010;125(2 Suppl 2):S33–S40.
23. Krampera M, Cosmi L, Angeli R, et al. Role for interferon-gamma in the immunomodulatory activity of human bone marrow mesenchymal stem cells. Stem Cells. 2006;24(2):386–398.
24. English K, Barry FP, Field-Corbett CP, Mahon BP. IFN-gamma and TNF-alpha differentially regulate immunomodulation by murine mesenchymal stem cells. Immunol Lett. 2007;110(2):91–100.
25. Liu X, Zhao M, Wu K, et al. Immunomodulatory and anticancer activities of phenolics from emblica fruit (Phyllanthusemblica L.). Food Chem. 2012;131(2):685–690.
26. Ogechukwu OE, Ogoamaka OP, Sylvester NC, et al. Steroids and triterpenoids from Eastern Nigeria mistletoe, Loranthusmicranthus Linn. (Loranthaceae) parasitic on Kola acuminata with immunomodulatory potentials. Phytochem Lett. 2011;4(3):357–362.
27. Arya V, Gupta VK. A review on marine immunomodulators. IntJ Pharm Life Sci. 2011;2(5):751–758.

Corresponding Author

Vikrant Jain*

Department of Chemistry, Madhyanchal Professional University, Bhopal 462044, India

www.ignited.in