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Molecular Docking Studies of Important Vitamin as Inhibitors Against Cytokine Target

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Abstract

Interleukins are a group of cytokines, small proteins that play an important role in immune and inflammation systems expressed by white blood cells (leukocytes). Interleukin (inter- as communication and -leukin as leukocyte) were associated with its specific code number. Vitamins are found to restore the ability of some cells to produce specific cytokines. This docking study aims to quantify the binding affinity or chemical bonding strength of vitamins at several interleukins using PyRx computational chemistry software. Macromolecules structures were fetched from The Research Collaboratory for Structural Bioinformatics Protein Data Bank (RCSB PDB) database, while small ligands were downloaded from PubChem of the National Center for Biotechnology Information (NCBI). The research concludes that folic acid (Vit B9), ergocalciferol (Vit D2), cholecalciferol (Vit D3), menatetrenone (Vit K2), tocotrienol (Vit E family) were five vitamins (of as many 21) which have the strongest average bonding affinity computed to 11 types interleukins, with the score -7.43, -7.27, -6.83, -6.81, and -6.72, consecutively. The research is useful as a preliminary attempt to obtain the number of vitamins that are important in the immune system.

Keywords: Vitamin, Interleukins, cytokines, pyrex.

INTRODUCTION

Interleukin ("between leukocytes") are molecules that mediate communication between various types of cells, firstly expressed by leukocytes (white blood cells) alone. When produced, interleukin, which consists of a large group of proteins that can elicit many reactions in cells and tissues by binding to high-affinity receptors in cell surfaces, travels and binds to the receptor in the surface of its target cell. Interleukins play an essential role in the activation and differentiation of immune cells and also for proliferation, maturation, migration, and adhesion with pro-inflammatory and anti-inflammatory properties (Justiz Vaillant & Qurie, 2021).

Interleukin consists of several families according to its gene nomenclature, which is grouped according to its ability to induce specific T-cell differentiation pathways. More than 60 interleukins (IL) have been characterized, including the list from IL-1 to IL-39, interferons (IFN), and tumor necrosis factor (TNF) family members (Bernardi et al., 2018). Interleukin is a subgroup of cytokines, i.e., chemokines that serve as chemotactic agents or chemoattractants for other cells. IL-1β, IL-6, and IL-8 are key pro-inflammatory interleukins that can activate the immune system

and contribute to the acute inflammatory response. IL-10 can inhibit the production of pro-inflammatory cytokines by activation of T (thymus) cells and monocytes (Garth et al., 2018).

Vitamins are micronutrients molecules that occur naturally or chemically synthesized that are required in trace amounts for the maintenance of the human body's metabolism. Some vitamins such as B and C are water-soluble vitamins which retained in normal subject blood plasma (Odum & Wakwe, 2012), whereas fat-soluble vitamins, e.g., A, D, E, and K, are absorbed into blood plasma and stored in the fatty portion of organs, particularly in muscle, heart, and liver (Jang et al., 2020).

Some major vitamins act as antioxidants to boost up immune response by strengthening the activity of immune cells during pathogenic microorganism attack, upon entry of some toxic materials either from inhaled air from respiration, ingestion of food, or from the skin or open wound (Irfan & Aslam, 2017).

The research aims to find vitamins that have the highest effect on interleukin as a receptor initiates and activates the immune system.

METHODOLOGY

The molecular docking technique was performed on several vitamins with various interleukins. Macromolecules structures data set were fetched from The Research Collaboratory for Structural Bioinformatics Protein Data Bank (RCSB PDB) database, while small ligands were downloaded from PubChem of National Center for Biotechnology Information (NCBI).

PyRx version 0.8, equipped with AutoDock Vina wizard, computational chemistry software, is used to quantify binding affinity or chemical bonding strength of vitamins at interleukins (Trott & Olson, 2010). The calculation was done with nine replications. Simulation is done using a personal computer with Intel(R) Core (TM) i5-2400 CPU @ 3.10GHz 3.10 GHz, with 4,00 GB RAM, 64-bit operating system, and x64-based processor.

RESULT AND DISCUSSION

Molecular docking is expressed as binding affinity or binding energy (kcal/mol), where more negative indicates a stronger bond. All of the vitamins with a total 21 variance were successfully docked to 11 interleukins (included TNF-α cytokine). The result of the docking study is presented in Table 1 shows the binding affinity value of vitamins averaged from each interleukin.

Table 1: Binding affinity (kcal/mol) of vitamins in average to 11 types of interleukin as target receptor

Vitamins	Alias	Average Binding Affinity (Kcal/mol)
Folic acid	B9	-7.43
Ergocalciferol	D2	-7.27
Cholecalciferol	D3	-6.83

Menatetrenone	K2	-6.81
Tocotrienol	E	-6.72
Riboflavin	B2	-6.45
Retinal	A	-6.32
Phylloquinone	K1	-6.13
Tocopherols	E	-6.07
Thiamine	B1	-5.12
Biotin	B7	-4.94
Salicylic acid	S	-4.89
Anthranilic acid	L1	-4.76
Pantothenic acid	B5	-4.75
Ascorbic acid	C	-4.73
Pyridoxamine	B6	-4.64
Pyridoxal	B6	-4.61
Pyridoxine	B6	-4.61
Niacinamide	B3	-4.41
Nicotinic acid	B3	-4.37
S-Methylmethionine	U	-3.88

From Table 1 above, it is shown that folic acid (Vit B9), ergocalciferol (Vit D2), cholecalciferol (Vit D3), menatetrenone (Vit K2), tocotrienol (Vit E family) were five vitamins (of as many 21) which have strongest average bonding affinity computed to 11 types interleukins, with the score -7.43, -7.27, -6.83, -6.81, and -6.72, consecutively. The research is useful as a preliminary attempt to obtain the number of vitamins that are important in the immune system.

On the opposite side of the viewpoint, in search of which interleukins respond most to vitamins, the result in Table 2 showed that TNF-α, IL-23, and IL-12 had a stronger binding affinity to an average of 21 vitamins.

Tumor Necrosis Factor Alpha (TNF-α) is an inflammatory cytokine produced by macrophages/monocytes during acute inflammation. TNF-α is important for resistance to infection and cancers (Idriss & Naismith, 2000). IL-23 functions in innate and adaptive immunity and is a key cytokine for promoting inflammatory responses in a variety of target organs (Tang et al., 2012). Interleukin-12 (IL-12) is a heterodimeric pro-inflammatory cytokine that regulates T-cell and natural killer-cell responses and is an important link between innate resistance and adaptive immunity (Vecchio et al., 2007).

Table 2: Binding affinity (kcal/mol) of averaged vitamins to each type of interleukin

Interleukins	Alias	Average Binding Affinity (Kcal/mol)
2AZ5	TNF-α	-6.28
3D87	IL-23	-5.86
1F45	IL-12	-5.73
4HR9	IL-17a	-5.69
5N92	IL-17AF	-5.58
2H24	IL-10	-5.54
1IAR	IL-4	-5.46
9ILB	IL-1β	-5.34
4MHL	IL-11	-5.2
1N1F	IL-19	-5.18
1M47	IL-2	-4.76

CONCLUSION

Folic acid (Vit B9), ergocalciferol (Vit D2), cholecalciferol (Vit D3), menatetrenone (Vit K2), and tocotrienol (Vit E family) showed the strongest binding affinity in average to interleukins. This result might be used for further research while working on the inflammatory setup as consideration, although an in-vivo study should be done. The finding suggests marking these vitamins as important vitamins for anti-inflammatory.

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