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International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

A COMPREHENSIVE REVIEW OF PTERIDINE DERIVATIVES

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ABSTRACT:

Pteridines are a group of heterocyclic compounds which contain nitrogen as a major heteroatom and it was aromatic compounds that are attached to pyrazine and pyrimidine ring families. Pteridine derivatives have focused on a specific place in the medicinal chemistry field. Pteridine ring is present in several natural compounds such as Pterin, Hemiptera (erythropoietin), Biopterin, Neopterin, Xanthopterin, iso-xanthopterin, etc.., which include a few heterocyclic compounds like pyrimidine, pyrazine rings. Some vitamins like folic acid and riboflavin and drugs like methotrexate and triamterene contain pteridine nucleus. This review article shows collective information about various pharmacological activities of pteridine and its derivatives like Antineoplastic, Anti ischemic, Antioxidant, Anti-inflammatory, Antidiuretic, Anti-microbial, Antihypertensive, Antitumor, etc, activities.

KEYWORDS: Pteridine, Pharmacological activity, Methotrexate, Triamterene.

INTRODUCTION:

In Pharmaceutical Chemistry, the druggist tries to design and synthesize a drug or a medicine or a pharmaceutical agent, which can be well-being kindness. Heterocyclic chemistry or ring structure is cyclic compounds that contain at least 2 different atoms such as Carbon and more than another element. Nitrogen, Oxygen, and Sulphur are the most used heteroatoms. These heterocyclic compounds are broadly separated in nature. The chemistry of heterogenous bicyclic compounds is the most vital within the figure out newly developed drugs and extensive medicinal properties.

PTERIDINE:

Pteridines (pyrazino[2,3-d] pyrimidine) compounds, (fig.1) are a class of heterocyclic compounds of combination by the six-member ring that contain two nitrogen atoms and four carbon atoms.

Pteridine [1] is an aromatic chemical compound, Molecular formula $C_6H_4N_4$, Molecular weight 132.12, which is soluble in cold water and other polar solvents. It is a yellow color in nature and volatile however odourless. It can be crystallized along-with alcohol like methanol and ethanol, benzene, or light petroleum when it is in a different form. It's composed of a group of heterocyclic compounds that is fused pyrazine and pyrimidine compounds. They have diverse numerous biological roles. These heterocyclic compounds are formed by many ecosystems, wherever they exhibit various biological and organic living functions. A various natural compound like Hemiptera (erythropoietin), which is red. There are different subclasses of pteridine derivatives. Some vitamins of the B series like folic acid (Vit B12) and riboflavin (Vit B2) [2] and drugs like methotrexate and triamterene contain pteridine nucleus. A pteridine is also called azinepurine,1,3,5,8-tetraazanaphthalene.

Pteridine derivatives have concentrated on a certain place in the pharmaceutical chemistry field. Natural found pteridine ring compounds especially: pterins, lumazine, and isoalloxazine. Thus, all living organisms have maintained and shared the same metabolic synthesis pathway through growth development.

Figure no.1 Pteridine

PHARMACOLOGICAL ACTIVITY:

The pharmacological activity of pteridine shows such as Antineoplastic[3], Antioxidant, Anti-inflammatory[4], Antibacterial[5], Antiviral[6], Antifungal[7], Antileishmanial [8], Antidiuretic[9], Antihypertension[10], Antiparasitic[11], Antimalarial, Hepatoprotective[12], and neurodegenerative agents as well as alpha-tumor necrosis factor agents[13], lipoxygenase inhibitors, xanthine oxidase inhibitor[14], nitric oxide inhibitor[15] and adenosine kinase inhibitors[16] and it is useful in biology as a support component of different nucleotides or nucleosides.

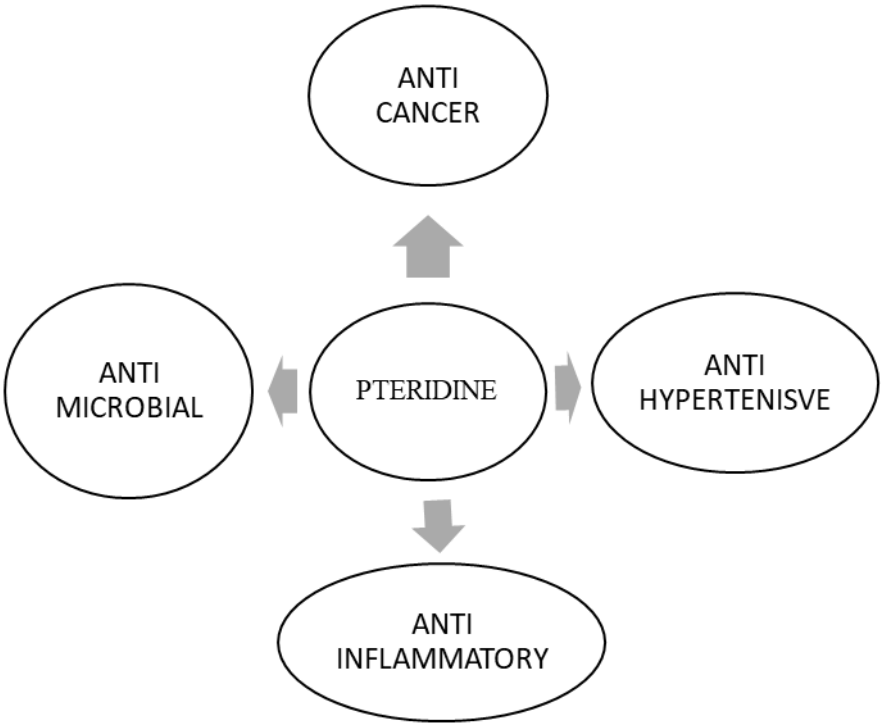
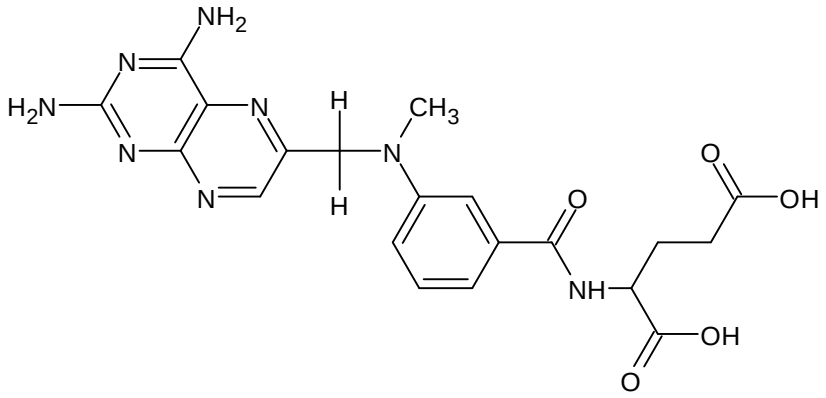


Figure 2: Major activities of Pteridine

ANTICANCER ACTIVITY:

In all parts of the world, the first and foremost cause of death is heart failure. Cancer is the second leading cause of death, with an ever-increasing incidence [3]. Hence, there is a need for more systematic treatment to reduce the adverse effects of current treatments and nullify tumor cell resistance. In this sense, compounds having the ability to inhibit the formation of tumors have been studied to search for novel anticarcinogenic drugs. Pteridine derivatives have the capability of anti-tumor action. Their derivatives are interesting in the heterogenous targeted molecules and mechanisms of protein.

Methotrexate,[17] also known as amethopterin (2,4-[(2,4-diaminopteridin-6-yl)-methyl-methylamino] benzoyl] amino] pentane dioic acid), is an anticarcinogenic drug, folic acid antagonist, and immune suppressant. The mechanism of this drug binds with the enzyme dihydrofolate reductase (DHFR) [18] and hinders the folic acid from making DNA and may kill cancer cells. Complications of this drug are bumps, erythema, and pain. Methotrexate is a sort of rheumatoid joint pain reliever and folacin's enemy. MTX was used as an antineoplastic drug during the olden days, further alone or in combination with any other neoplastic agents to analyse cancer of the breast, cutaneous T cell malignancy, lymphocytic disorder, acute myeloid leukaemia, lung carcinoma, and elaborated stages of non-Hodgkin’s lymphoma.

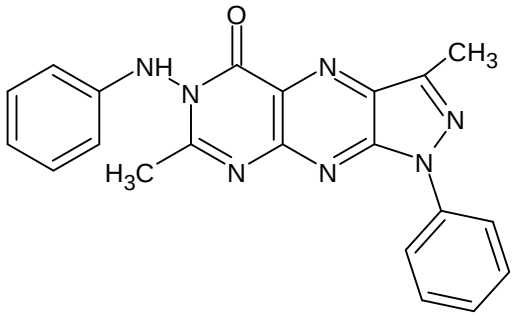


Methotrexate

ANTI-INFLAMMATORY ACTIVITY:

Inflammation is the body's natural protector against injury or infection. Inflammation is an immune cycle triggered by the presence of non-toxic or damaged tissues [4]. Through the path of inflammation, the production of signal molecules such as cytokines and the recovery of immune cells help to remove pathogens and restore tissues. However, most of the actions are directed to kill pathogens and/or destroy dead cells, which can also damage normal cells.

In various disorders, such as rheumatoid arthritis, the allergic disorder of respiration (asthma), or hepatic cirrhosis, the inflammatory process is dysregulated and continuously active, leading to chronic infection. To decrease inflammation, nonsteroidal anti-inflammatory drugs (NSAIDs) are commonly used, but due to their collateral effects, they are not prescribed to treat chronic diseases. A sequence of pteridines and their derivatives compounds were produced and estimated for activities of antibacterial and anti-inflammatory [19].

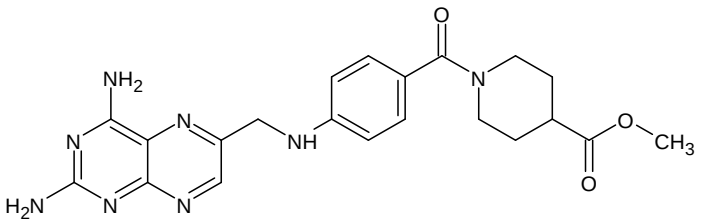


6-anilino-3,7-dimethyl-1-phenyl-1,6-dihydro-5*H*-pyrazolo[4,3-*g*] pteridin-5-one

ANTI-PARASITE ACTIVITY:

Protozoan parasite Leishmania causes a disease called leishmaniasis [8]. It is transferred by infected phlebotomine sandflies. It is a climatic disease allied to vitamin and protein deficiency; thus, it mostly affects under-developed countries. Leishmania is a folate auxotroph8, and Dihydrofolate reductase (DHFR) is complicated in the case of anemia (low folate). They have various strategies that have been directed to prohibit protozoan Leishmania parasite growth and development along with pteridines.

In trypanosomiasis, the parasite Trypanosomatidic [21], the thymidylate synthase zone is coupled to an N terminal DHFR zone, illustrating its role as a dual functional impulse. As a result, DHFR inhibitors have only had a minor anti-leishmanial effect. Therefore, new treatments have been developed to hinder that action on humans and parasites. These anti-parasite activity studies consider pteridine substituted compounds that have p- aminobenzoic acid (PABA) as an addition to that compound by in vitro enzyme inhibition, which can block Leishmania major PTR1[22] while weakly influencing human DHFR.

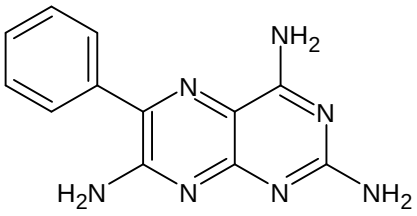


ANTI HYPERTENSION & ANTIDIURETIC ACTIVITY:

Hypertension (High blood pressure):

Blood pressure is the force that makes an effort by passing blood as opposed to the walls of the body's arteries. Hypertension is when blood pressure is too high. Hypertension is also referred to as cardiovascular disease. In public health, Hypertension is one of the significant challenges globally. It's a high risk of many disorders together, such as stroke, heart failure, coronary artery disease, and retinopathy.

Triamterene (6-phenylpteridine-2,4,7-triamine) is the pteridine-triamine subsidiary. This drug acts as a diuretic drug. Triamterene is a sort of potassium-sparing diuretic [23]. Normally, in the collecting duct of the kidney, it acts as a preventing agent of sodium resorption. At the same time, the triamterene drug that deals with predominantly passing out more fluid, the activity of the sodium-potassium exchange pump (Na-K ATPase) has been hindered, which prompts the discharge of ions of sodium and water. At the same time, it reduces potassium (K^+) particle disposal within the distal convoluted tube (DCT) and the gathering ducts of the urinary organs within the uriniferous tubules. This compound is frequently utilized in combination with a thiazide derivative (hydrochlorothiazide) as a diuretic/hypertensive medication since their actions are synergetic. The diuretic activity was assessed in Wistar rats which test compounds (furosemide or triamterene) ratio of Na^+ concentration was determined [24].

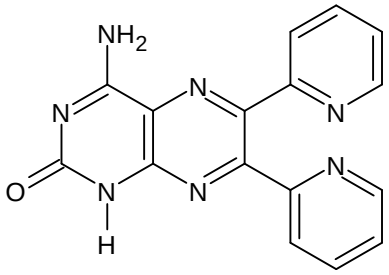


Triamterene

ANTIMICROBIAL ACTIVITY:

Antimicrobial activity signifies the process of killing or inhibiting disease-causing microbes. For this purpose, different antimicrobial agents are utilized. Antimicrobials may be antibacterial [25], anti-fungal, or antiviral. All of them have various modes of action that act to suppress the infection. Although the number of freshly developed antibiotic agents has slightly risen, there is still a need for new antibiotics because of the unavoidable growth and development of microorganism resistance, which has led to the appearance of bacteria with unsuccessful chemical treatments.

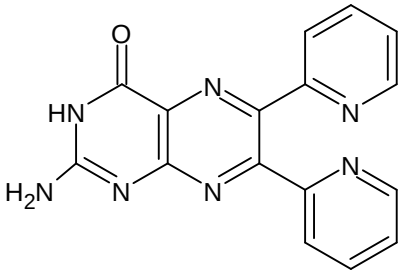
A distinct sequence of pteridine was estimated to show their possible bactericide action. To identify drugs that can inhibit E. coli DNA topoisomerase I [26], this enzyme would block DNA double-strand re-joining, which causes the improvement of deoxyribonucleic acid (DNA) cleavage that lowers cell viability and pteridine derivative compounds can attach to fragments of DNA and RNA and quelate. Among the evaluated compounds, dipyridine-pteridine derivative showed that it created a restraint zone against E. coli bacteria, which displays maximal bactericide potential.



4-amino-6,7-di(pyridin-2-yl) pteridin-2(1*H*)-one

ANTIFUNGAL ACTIVITY:

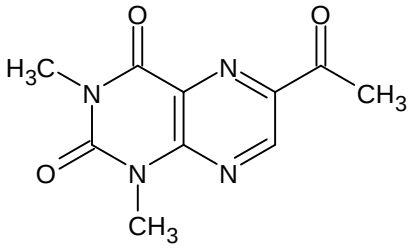
An antifungal agent is utilized to treat and prevent mycosis (caused by fungi such as ringworm). The antifungal activity [27] of pteridine has been concentrated. Thus, 2-amino-6,7-di (pyridine-2-yl) pteridine-4 (3*H*)-one reached the diameter of the inhibition zone over against C. Albicans and C. tropicalis. A few mixtures from the sequence of pteridine-dipyridyl have likewise shown antifungal properties. This work on fungal infection shows that sequence pteridine substitutes have fungal treating activity.



2-amino-6,7-di(pyridin-2-yl) pteridin-4(3*H*)-one

ANTIVIRAL ACTIVITY:

A virus is a naked micro-organism infectious medium that can fluently spread. agents which are used to detect, remove or protect against viruses. Instead, they inhibit its development. Most antimicrobial and antiviral drugs don't obliterate their micro-organisms. That primary treatment strategy consisted of binding assays on nucleic acid [28] via electrophoresis, observed by an ex-vitro assay. Novel pteridine and its subordinates have been synthesized in the sought-after antiviral medication. A few mixtures from the sequence have likewise shown antiviral properties.



6-acetyl-1,3-dimethyl-4a,8a-dihydropteridine-2,4(1*H*,3*H*)-dione

CONCLUSION:

In conclusion, these show the effect of any changes in substituent in pyrazine or pyrimidine ring which formed. They display various pharmacological functions. There is a newly grown interest system of together for bicyclic heterogeneous compounds. This overall review article is purpose to discuss pharmacological activities of pteridine and its derivatives mainly stand for pure chemistry.

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