



## Pteridine a Colored Heterocycle and Its Anticancer activity: (An Overview)

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### ABSTRACT

The objective of this work is to provide an overview of the numerous pharmacological features that are associated with the pteridine molecule. Pteridines are nitrogen-containing heterocyclic compounds that are well-known and noteworthy. Their chemical formula is  $C_6H_4N_4$ . In recent years, pteridine's various potential uses in the field of medicinal chemistry research have garnered significant attention. In the expanding field of intensive study, Pteridine is regarded as a privileged scaffold, and the alteration created with diverse substituents around the centroid opened the way for researchers to deal with it at ease. The heterocycle, which is a fused ring, has a high pharmacological quality. A pteridine is one of the heterocycles that has attracted a lot of interest in terms of biological uses. The pteridine nucleus serves as the quintessential framework in a range of physiologically energetic chemicals and pharmacological molecules. This evaluation is necessary in order to bring to light the remarkable potential that this ring device possesses as a result of the wide variety of pharmacological effects it may perform. This research might unquestionably hasten the graph and synthesis procedures, which would ultimately yield in a wide array of therapeutically feasible medicinal options.

**Keywords:** Pteridine, Anti-tumour, Cancer Cell-lines, Tumourgrowth.

### INTRODUCTION

Chemists in medicinal chemistry strive to create, investigate, and manufacture medications or drugs that will help humanity. The chemistry of heterocyclic molecules is critical in the development of novel medications. A pteridine is an aromatic heterocycle that results from the reaction of

pyrimidine with pyrazine. Pteridine derivatives are mostly obtained from insects wings, (Pterones means wings in Greek).<sup>1</sup> Pteridine, basic nucleus are yellow in colour and its derivatives are mostly coloured compounds. Compounds made up of fused pyrimidine and pyrazine rings. Pteridine research has long been recognized as critical to many biological processes, that includes amino



acid metabolism, synthesis of various nucleic acid, neurotransmitter production, chemotherapy of cancer, cardiovascular function, and the overall necessity of practically all living species.<sup>1</sup> Analgesic, anti-inflammatory, anticonvulsant, sedative-hypnotic, anti-histaminic, anti-hypertensive, anti-tumor, anti-microbial, ischemia or reperfusion surgery, and anti-parasite activity are some of the pharmacological responses ascribed to these systems.<sup>2</sup> This diversity in the pharmacological action contours of pteridine has piqued the interest of medicinal chemists in exploring this fused Heterocycle's potential against a wide range of activities.

### Pteridine

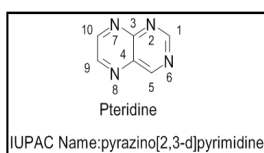


Fig. 1.

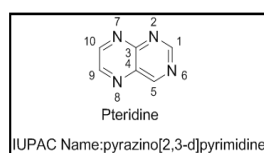


Fig. 2.

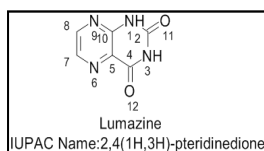


Fig. 3.

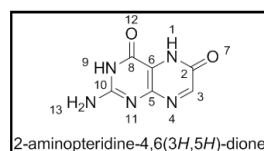


Fig. 4.

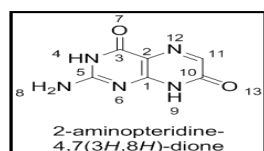


Fig. 5.

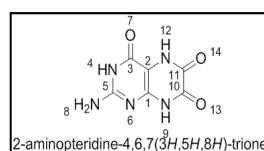


Fig. 6.

The name pteridine refers to the pyrazino [2,3-d]pyrimidine nucleus suggested by scientist Wieland in 1941. The IUPAC regulations govern the nomenclature of this fused-ring system; however, the central CTC bond may be replaced. Because the pyrimidine moiety of the nucleus of pteridines found naturally has the same pattern of substituents, it has been widely accepted to call 2-amino-4(3H)-pteridine 'pterin.'<sup>3</sup>As a result, this phrase is frequently employed as a distinguishing feature of the common name of naturally occurring pteridine compounds. Similarly, the 2,4(1H,3H)-pteridinedione derivatives **3** are referred to as 'lumazines.' Prefixes such as "dihydro-," "tetrahydro-," and so on are used to indicate reduced compounds. The numbers following the prefixes represent the locations of the additional hydrogen atoms in nucleus. In pteridine derivatives, tautomerism is prevalent, and the structural formulae should represent the preferred tautomers in them. Amino groups do not exist in the iminodihydro form, but hydroxy and thiol functionalities **9** near or at the para position to a ring nitrogen atom favoramide (lactam) and thioamide (thioxo) configurations, which are thermodynamically more stable.<sup>1,2</sup>

### Physical properties<sup>4</sup>

1. Pteridine yellow-colored is a solid material.
2. Melting Point: 139.5°C.
3. It is soluble in water
4. Log log-logp: -0.58

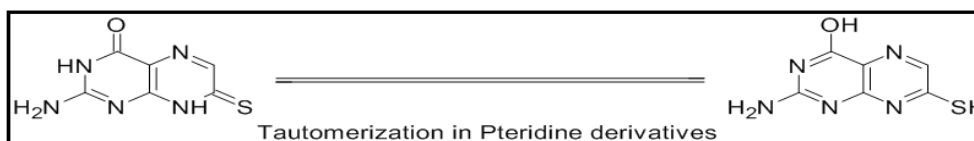


Fig. 7.

### Method of preparation

Gabriel-Isay (Gabriel-Colman) synthesis: Pteridines are synthesized via cyclo-condensation

of 5,6-diaminopyrimidine with benzil or glyoxal to get 4-methyl-6,7-diphenylpteridine. This reaction is also known as the Gabriel-Colman synthesis.<sup>5</sup>

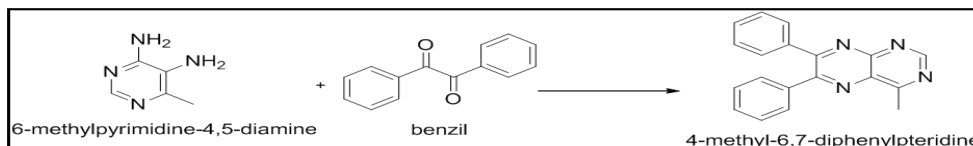


Fig. 8.

On the other hand, when diamino-pyrimidine was reacted with diketones, keto aldehydes, keto acids, which are

unsymmetrical in nature or their esters, a number of different pteridine derivatives were produced.<sup>5</sup>

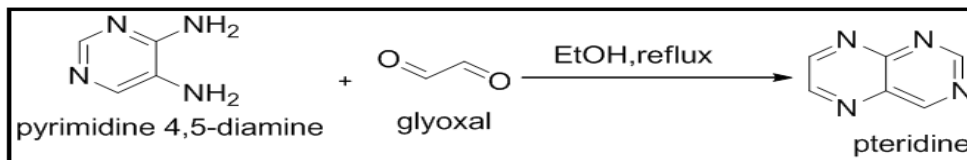


Fig. 9.

### Polonovski-Boon reaction

In synthetic procedure, when 6-chloro-5-nitropyrimidine reacted with an  $\alpha$ -aminocarbonyl

molecule yields an intermediate, resultant product 2-amino-6-methyl-7,8-dihydropteridin-4(3H)-one is obtained after reduction and cyclization.<sup>6</sup>

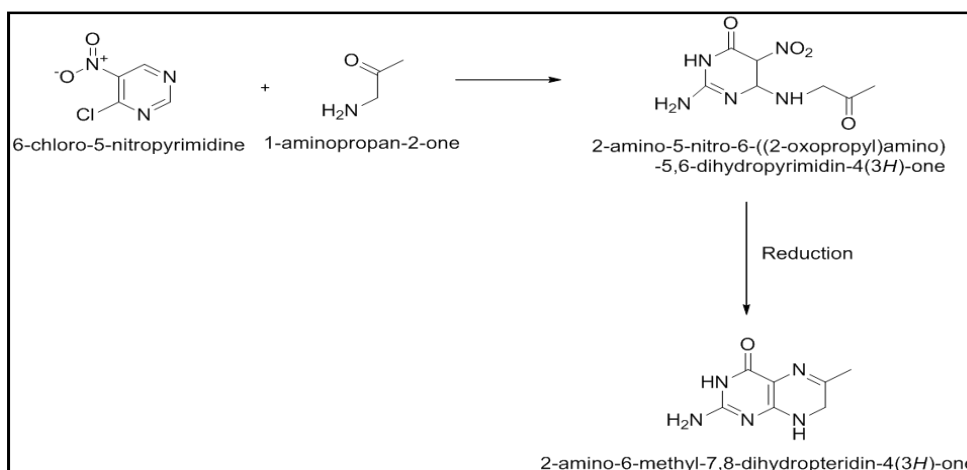


Fig. 10.

### Timmis synthesis

Dehydration synthesis of 4-amino-5-nitrosopyrimidines via Base-catalyzed process with

molecules such as ketones, aldehydes, nitriles, and cyanoacetic acid, (Which have an activated methylene group,) results in condensed pteridines derivatives.<sup>7</sup>

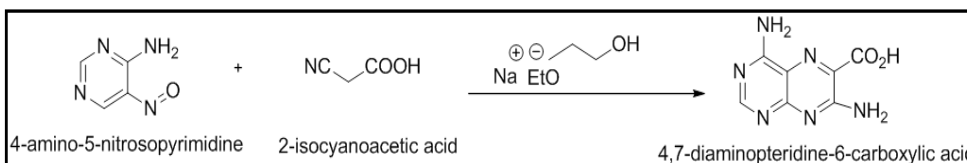


Fig. 11.

Condensation of  $\alpha$ -methylene nitrile with 5-nitropyrimidine-2,4,6-triamine

resulted in triamterene, a potassium-sparing diuretic.

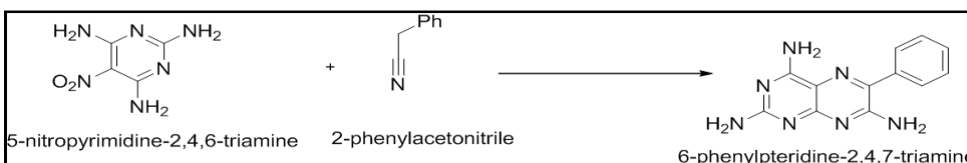


Fig. 12.

**Pachter synthesis**

The reaction is modified by reacting 4,6-diamino-5-nitroso-2-phenyl pyrimidine

with, benzyl methyl ketone, in the presence of potassium acetate to create 4-amino-7-methyl-2,6-diphenylpteridine derivative.<sup>8</sup>

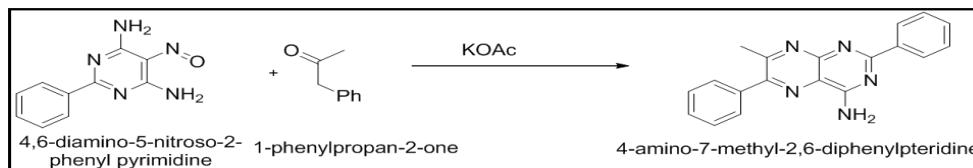


Fig. 13.

**Blicke synthesis**

When amino pyrimidines react with various aldehydes and hydrogen cyanide by

dehydration reaction followed by cyclization using Sodium methoxide as a base, leads pteridine derivatives via cyanoamines.<sup>6</sup>

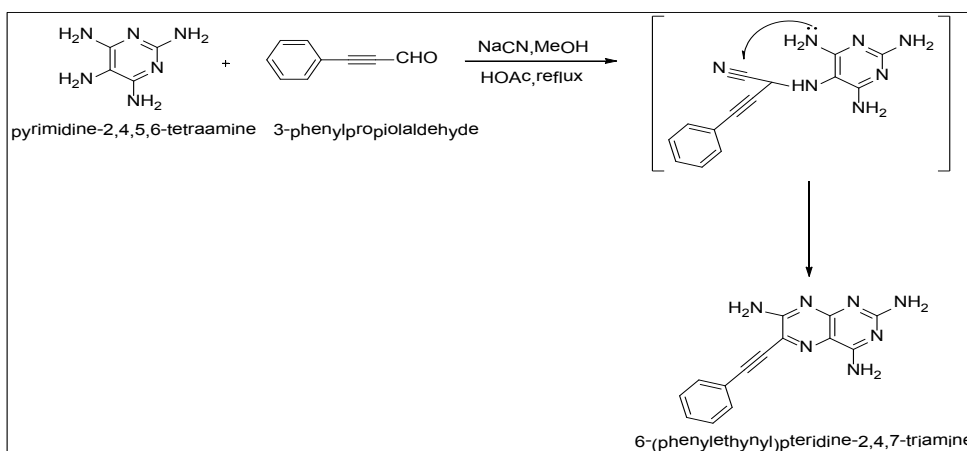


Fig. 14.

**From pyrazines**

The oxidative aromatization of 3-(amino-

methyl) pyrazin-2-amine with orthoformates results in 6-substituted pteridine.<sup>6</sup>

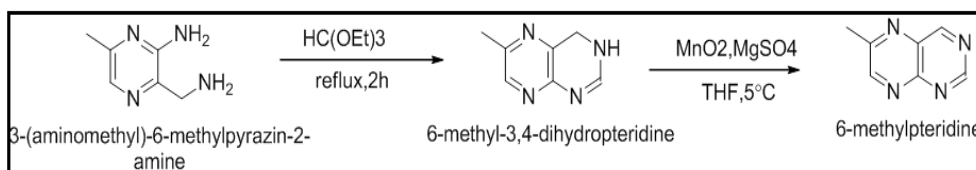


Fig. 15.

**Viscontini reaction**

Sugar phenylhydrazones condensed with 5,6-diaminopyrimidines under mild acidic

conditions, yielded 6-substituted pterins in this effective synthesis process which is regioselective in nature.<sup>6</sup>

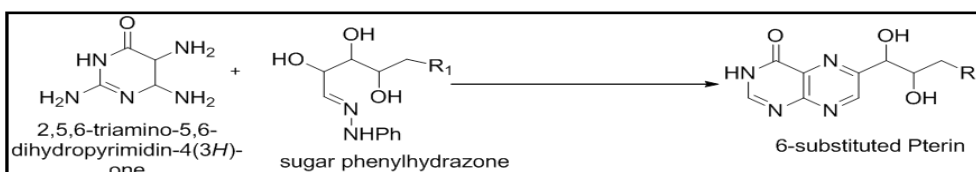


Fig. 16.

**Chemical Properties**

The pyrimidine ring of pteridine is sensitive enough and degrades with acid and alkali under the reaction circumstances. Heating 2,6-dihydroxypteridine with 100 percent sulfuric

acid at 240°C yielded 2-aminopyrazine; the same when undergoes heating (2,6-dihydroxypteridine) with 2–3 equivalents of 12 percent alkali for 2 h at 170°C yielded 2-amino-3-carboxylic acid. Both these acquired in substantial quantities.<sup>9</sup>

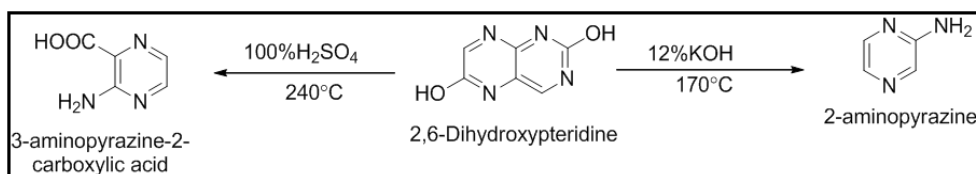


Fig. 17.

**Nucleophilic addition**

The fused Pteridine nucleus rapidly forms nucleophilic adducts with water, amines and alcohol, primarily at the C-4 and C-7 sites. Covalent

hydrates are formed via addition of water molecule to pteridine. Under acidic reaction environment, 3,4-hydrated cation forms first and gradually equilibrate with dehydrated 5,6,7,8-cation.<sup>10</sup>

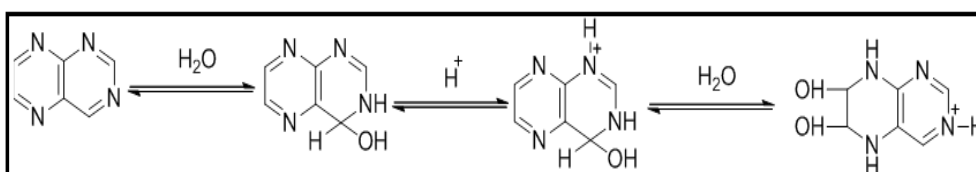


Fig. 18.

An equilibrium mixture of 3,4-dihydro-4-methoxypteridine and 5,6,7,8-tetrahydro-6,7-dimethoxypteridine are obtained when

A pteridine is nucleophilically added to methanol in the (1:1 adduct) and (2:1 adduct) respectively.<sup>6,10</sup>

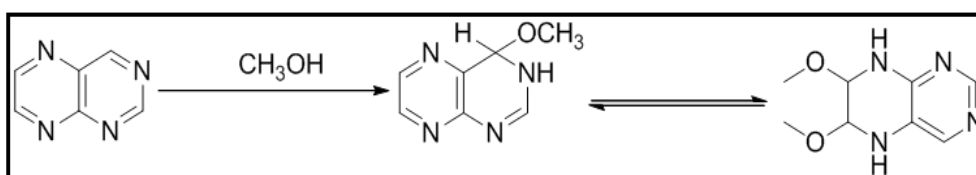


Fig. 19.

**Nucleophilic substitution reaction**

Using the pteridine in conjunction with the Grignard reagent, followed by oxidation, it is

possible to form a derivative with new carbon-carbon bond on the pyrazine ring of the nucleus, at the C-7 location of the ring.<sup>6</sup>

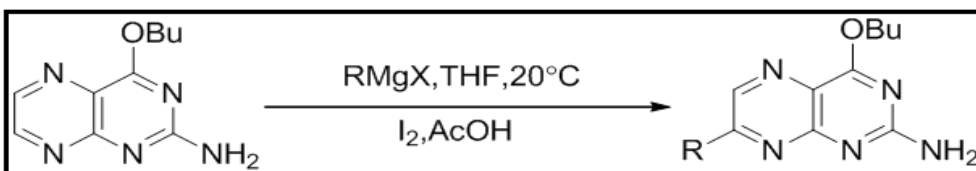


Fig. 20.

**Oxidation**

Pteridine derivatives, such as xanthopterin, are

transformed to leucopterin when preferably reacted to hydrogen peroxide or molecular oxygen over platinum.<sup>9</sup>

**Reduction**

Tetrahydropteridine derivatives are very reactive to oxidation, making isolation problematic. Availability of functional groups which are electron

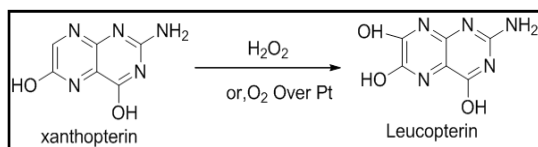


Fig. 21.

withdrawing in nature on the ring, provide separation easily. As a result of reacting properly substituted pteridine with sodium borohydride, 5,6,7,8-tetrahydro pteridine-4-carboxylate can be extracted.<sup>11</sup>

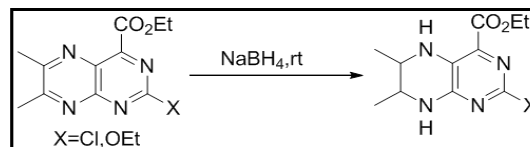


Fig. 22.

**Reaction with  $\text{PCl}_5$  and  $\text{POCl}_3$** 

Reactions which involve Leucopterin with very strong chlorinated agents like phosphorous

pentachloride and phosphorous oxychloride lead to form a substituted chloro derivative, which via reduction with hydroiodic acid generates 6-deoxyleucopterin.<sup>6</sup>

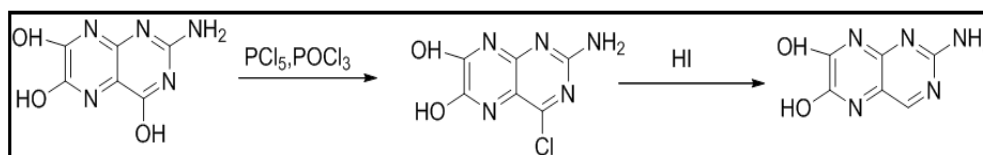


Fig. 23.

**Ring fission**

Pteridines have high thermal stability; nonetheless, they are unstable in hot

solutions. In aqueous acid, they fission the pyrimidine ring to produce 3-aminopyrazine-2-carbaldehyde.<sup>6</sup>

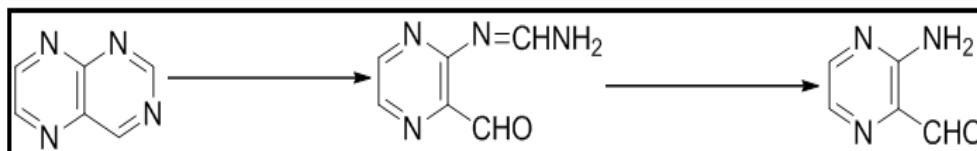


Fig. 24.

**Heck reaction**

The coupling reaction of 6-chloropteridine with acetylenes, mediated by palladium, produces

alkynyl substituted pteridines.<sup>12</sup>

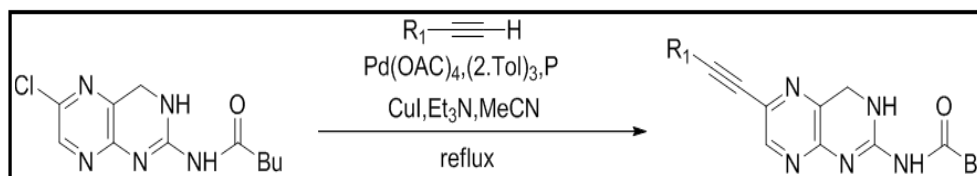


Fig. 25.

**Pharmacological scaffold**

Pteridine has a significant pharmacological impact because of its varied scaffold. For the previous decade, pteridine has been examined for its many aspects of impact to find the capability to create and isolate a range of

pharmacological activity.<sup>13</sup>

**Anticancer Activity**

Despite significant advances in early detection and treatment, cancer remains a primary health and social-economic concern.

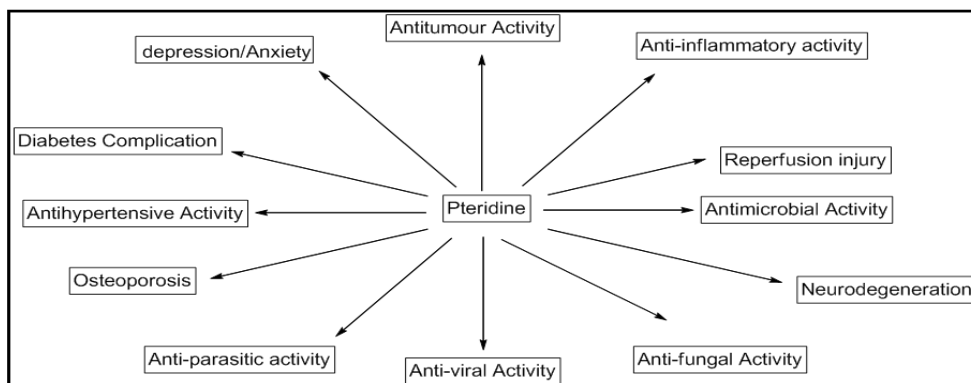


Fig. 26.

Cytotoxic drugs achieve their therapeutic effects by preventing the replication of DNA. Because cancer cells proliferate rapidly, they create a large amount of new DNA swiftly, which, if damaged, causes the cell to die. Interfering with DNA replication may be done with three different substances. Antimetabolites are substances that resemble nucleotides. Alkylating agents are substances that attach to DNA and change its structure permanently.<sup>14</sup> Regrettably, they also bind to a wide range of other substances in cells. Anthracyclines, antitumor antibiotics, platinum analogues, and some alkylating compounds are all examples of different types of DNA-binding drugs. DNA-binding antineoplastics are responsible for tissue damage because they promote deadly DNA crosslinking and strand breaks, both of which are induced by free radicals and ultimately result in cell death. These are often used in combination with an enzyme. Currently, cytotoxic medicines are utilized to treat cancer, either alone or in combination, and numerous of these medications are in various stages of clinical studies. These cytotoxic drugs have several drawbacks, including the inability to discriminate between malignant and normal cell types; a target-specific effect that is necessary for

increased treatment success; and as a result, they can cause serious adverse reactions to the recipient, which are usually cumulative and dose-limiting. Because of the emergence and dissemination of multidrug resistance to many conventional medications, as well as the ongoing significance of healthcare spending, a significant number of researchers have concentrated their efforts on the development and testing of novel and efficient anticancer drugs. A pteridine is a scaffold that is commonly utilized in bioactive compounds.

Several pteridine compounds have been licensed for clinical use as anticancer medicines by the Food and Drug Administration (FDA). Methotrexate, Pralatrexate are approved two examples for the same.<sup>15,16</sup>

Various cancer treatment targets have been identified to provide more relevant and accurate treatments. A number of studies have been published in the literature concerning the discovery and development of innovative potential pteridine derivatives for cancer therapy.<sup>17,18</sup>

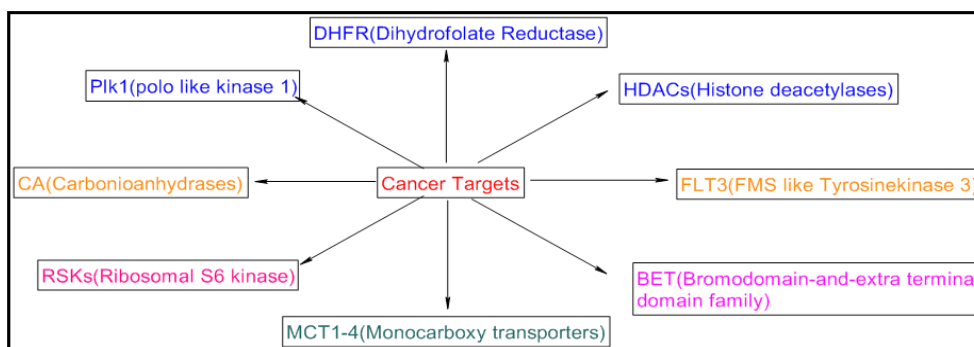


Fig. 27.

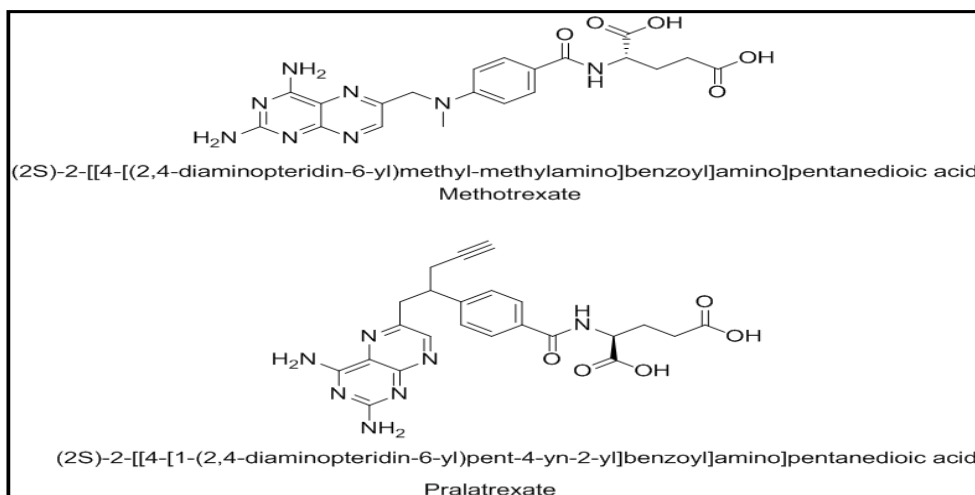


Fig. 28.

**Literature review**

Marques SM *et al.*, reported and synthetically prepared a novel Pteridine-sulphonamide conjugates, which act as carbonic anhydrases and dihydrofolate reductase inhibitors. Inhibition investigations were done on a group of CAs and DHFRs. Assays for

cell proliferation employing two types of tumor cell lines—1) A549 (adenocarcinomic human alveolar basal epithelial cells), 2) prostate carcinoma, PC-3). Among synthesized and analysed compounds, 1a and 4a were found to be the highest active, with KI of 4.5 and 260 nM, respectively<sup>19</sup>

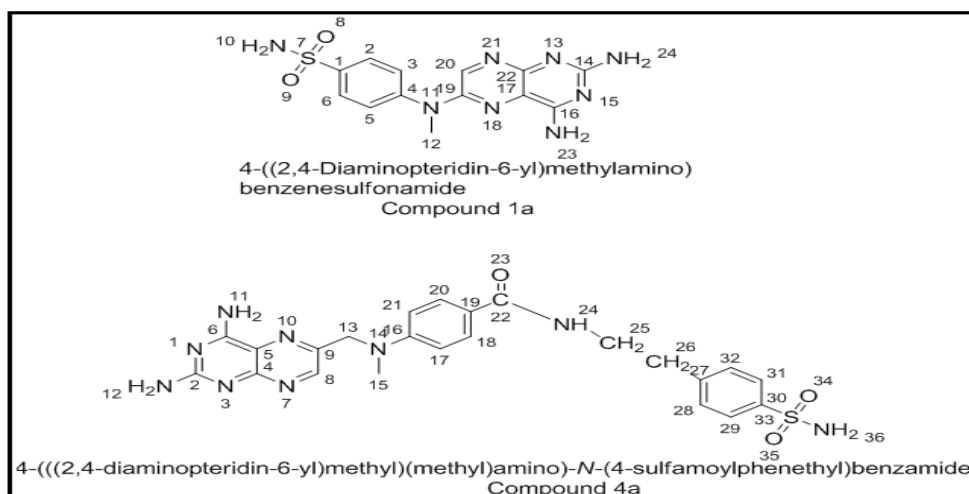


Fig. 29.

Liu KK *et al.*, reported a new sequence of 4-Methylpteridinones derivatives, which were further refined to increase their efficacy against PI3K $\alpha$  and mTOR targets. The availability of C4 methyl group is necessary for selectivity action because it matches the one-of-a-kind PI3K/mTOR binding pocket, whereas at the C6 position heteroaryl groups, improved PI3K

potency, according to SAR analysis. Both of these findings are based on the fact that the C4 methyl group fits the unique binding pocket. In a xenograft mouse model of U87 glioma cells, compound 2 was orally dosed (PI3K Ki = 2.8 nM and mTOR Ki = 6.8 nM), and found most effective one, demonstrating that treated animals' tumour volume was reduced by 25%.<sup>20</sup>



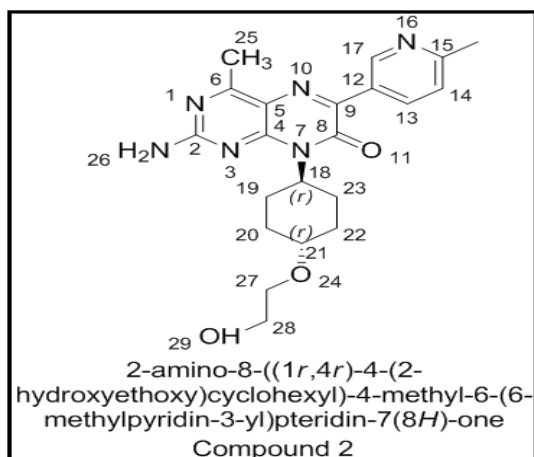


Fig. 30.

Wang H *et al.*, synthesized and

analyzed new Pteridine derivatives against the monocarboxylate transporter 1 (MCT1). In the majority of aggressive tumor types, MCT1 and MCT4 are substantially expressed, making them ideal targets for cancer therapy. Compounds 3 and 4a, respectively, were shown to inhibit the development of Raji Burkitt lymphoma cells expressing MCT1 but no other cell lines like MCT4 and MCF7 breast cancer cells engineered to overexpress murine MCT1. In these cells, Decrement of C-lactate transport which correlated with the antiproliferative effects in these cells. According to SAR analysis, Compounds 3 and 4a-c share a 1-naphthyl methyl or isobutyl substituent. In addition, these compounds have distinct hydroxyl groups in alkyl and thioether-containing tethers in their structures, It may have an important role in the action of these substances.<sup>21</sup>

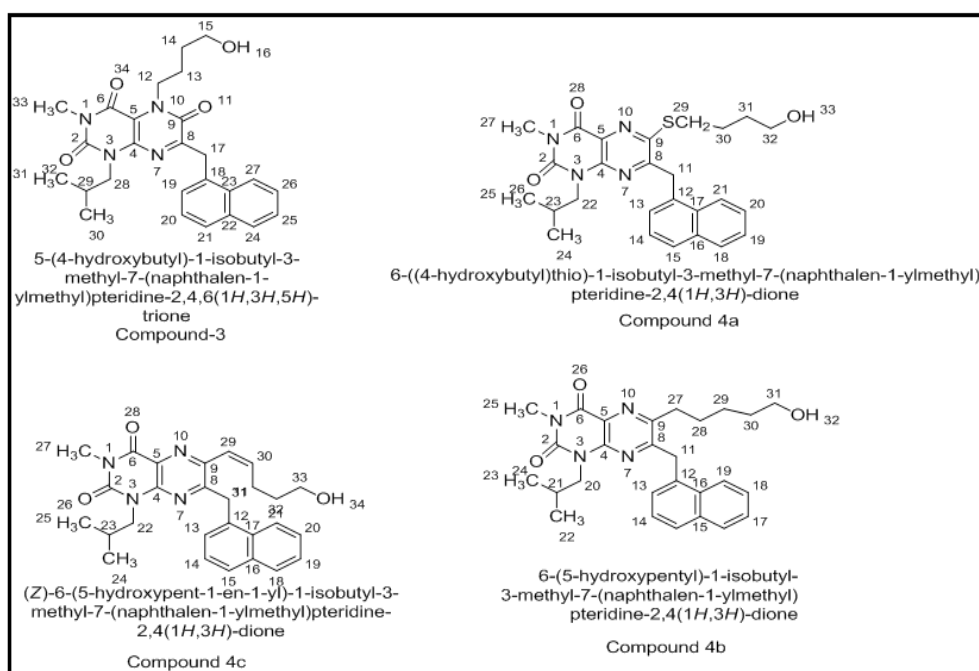


Fig. 31.

Okada L *et al.*, reported a series of novel Compounds based on pteridine7(8*H*). Compound 5 is the most structurally favorable of the produced compounds: containing, (1) the presence of a 4-methylpiperazinyl group and a methyl group in the phenyl substituent, and (2) the unavailability of a Michael acceptor in the aminophenyl radical. It was also evaluated on many cancer cell lines, including the AML cell line MV411, which carries

an FLT322 activating mutation often identified in AML patients ( $IC_{50}=51$  nM) Compound 5 was able to block the activity of FLT3-fms-like tyrosine kinase ( $IC_{50}=1.56$  nM,  $K_d = 0.25$  nM) as well as some of the enzyme's downstream signalling proteins. This reported derivative stopped the G0/G1 phase in the cell cycle and caused cell apoptosis in the MV411 xenograft mice model. It also inhibited tumour development.<sup>23</sup>

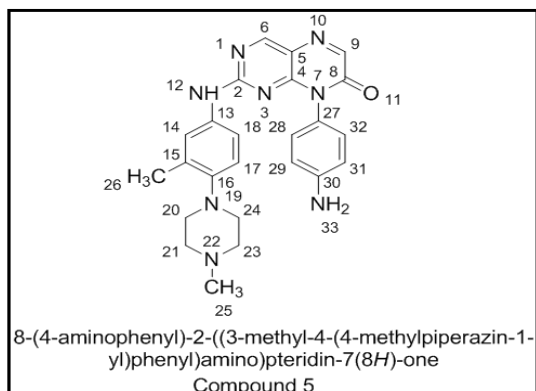


Fig. 32.

Hao Y *et al.*, reported and synthesized a focused, N5-Substituted 6,7-dioxo-6,7-dihydropteridines, Which are (EGFR) Inhibitors. Compounds were screened on T790M mutant and wild-type (WT) EGFR kinases, Among the synthesized compound, Compounds 6a and 6b were found active, with  $IC_{50}$  values 1.21nM and 3.82nM respectively on EGFR wild type cell line, besides this, they found effective on EGFRL858R/T790M cell line with particular  $IC_{50}$  value 0.68nM and 1.07nM and  $IC_{50}$  value 62.2nM and 59nM obtained for H1975 cell line.<sup>24</sup>

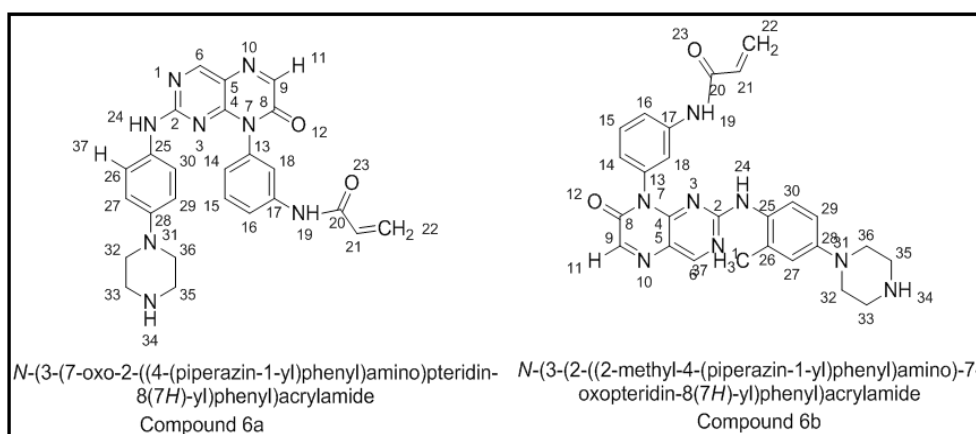


Fig. 33.

Shoji QA *et al.*, Synthesis and analyzed the Structure-Activity Relationship of 3-Hydroxypyridine-2-thione-base derivatives, synthesized derivatives tested as histone deacetylase (HDAC) inhibitors, The findings revealed that pterate-based hydroxamates were effective against a wide range of HDAC

isoforms, with five (8a) and six (8b) methylene groups providing the optimum linker length ( $IC_{50}$ =16.1 and 10.2 nM, respectively). Immunoblotting experiments demonstrated that the cytotoxicity was caused by the simultaneous inhibition of both the Histone deacetylase1 and Histone deacetylase<sup>6</sup> isoforms.<sup>25</sup>

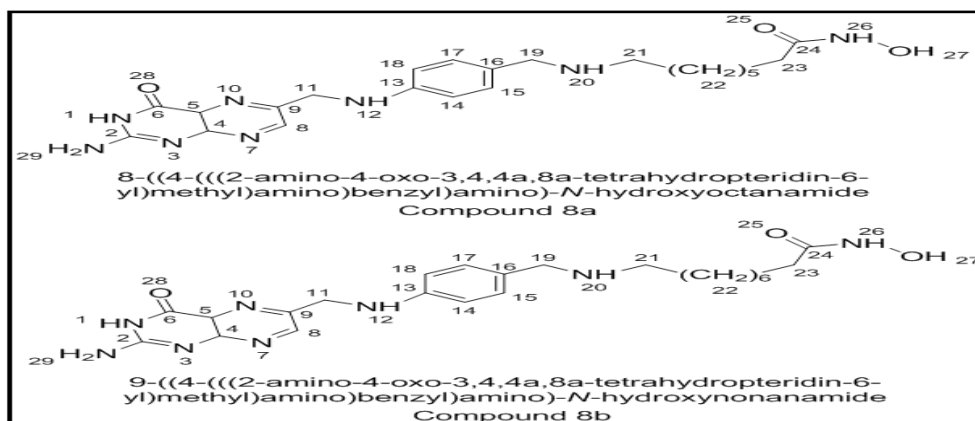


Fig. 34.

Nelson ME *et al.*, disclosed that 2-Amino-4-benzyl pteridine derivatives are effective inhibitors of the referenced alkyltransferase, however, the availability of DNA, reduced their inhibitory activity ( $IC_{50}=0.01$  to  $0.4 \mu\text{M}$ ). 4-benzyl folic acid (molecule 9) was the most potent among the derivatives tested. Additionally, the cytotoxic effect of 1,3-bis(2-chloroethyl)-1-nitrosourea (BCNU) was increased by these compounds when used against A549, KB(human epithelial carcinoma cells), and HT29(adenocarcinomic human alveolar basal epithelial cells) cells. ED90 of compound 9= $5 \mu\text{M}$  with BCNU  $40 \mu\text{M}$  were observed, which shows resistance to BCNU alone and more effective in cells that have greater levels of the  $\alpha$ -folate receptor expression.<sup>26</sup>

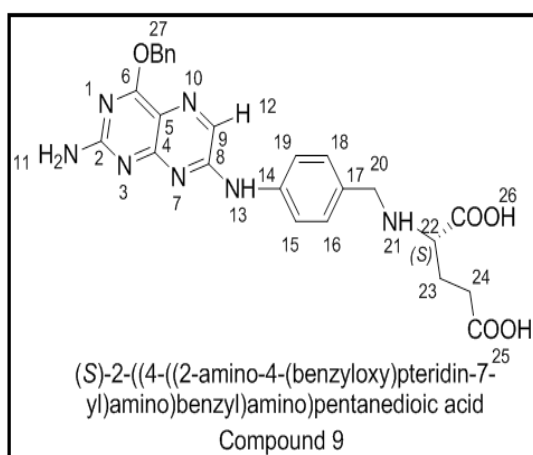


Fig. 35.

Rudolph D *et al.*, reported a of some new sequence of Polo-like kinase 1 (Plk1) inhibitors. Compound 10 inhibits Plk1 ( $IC_{50}=0.87 \text{ nmol/L}$ ) among the produced compounds. It was effective against number of tumours cell lines in several xenograft models and had significant tissue penetration. At 24 hours, BI6727 caused the cell cycle to remain in the G2/M phase, followed by apoptosis and an increase in sub-G1 peaks.<sup>27</sup>

Zhan MM *et al.*, reported a novel tetrahydropteridin chemical scaffold and screened on highly selective polo-like kinase2 inhibitors, Compounds C2 in  $3.40 \text{ nM}$  concentration against Plk2 and C21 in  $4.88 \text{ nM}$  concentration against Plk2, were found most promising among the produced compounds from the first and second series of selective Plk2 inhibitors, respectively. Furthermore, with selectivity values of 12.57 and 910.06, C21's selectivity over Plk1/3 was greatly boosted. K562, MCF-7(human breast cancer cell line), HuH-7(hepatocyte derived cellular carcinoma cell line), A549(adenocarcinomic human alveolar basal epithelial cells), H1975(exhibiting epithelial morphology), and HeLa cell lines were employed.<sup>28</sup>

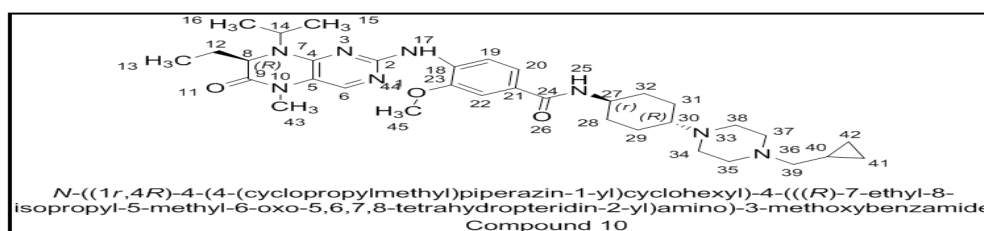


Fig. 36.

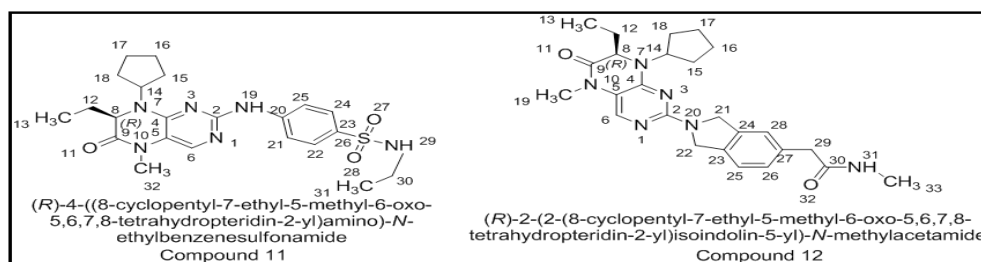


Fig. 37.

Kiryarov A *et al.*, synthesized and reported novel 5,6-Dihydroimidazo[1,5-f] pteridine derivatives, At 50nM, bound to Lys82 amino acid and reduced Plk1 activity. They made structural adjustments to the nitrile-containing compounds to enhance the ADME qualities in rats, resulting in compound 13. In xenograft animal models, this drug had a high microsomal stability, favoured the phosphorylation of histone H3, and had a excessive rate of absorption.<sup>29</sup>

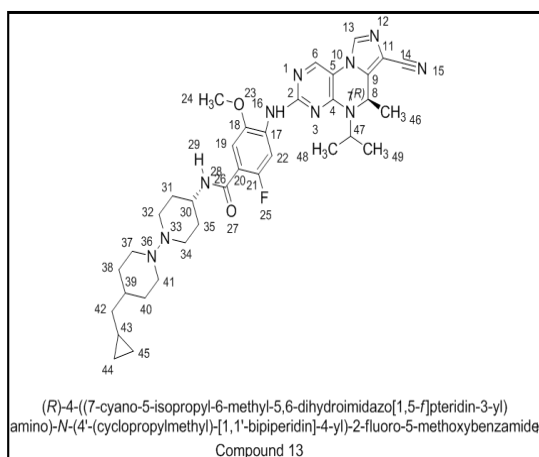


Fig. 38.

Koban LK *et al.*, reported some Tetrahydropteridine derivatives as aBRD4-selective(Bromodomain-containing protein 4) inhibitor. BRD4, which is responsible in a variety of biological actions including epigenetic control. Compound 14 was the most powerful, inhibiting BRD4 ( $IC_{50}=130\text{nM}$ ). When compound 14 was evaluated in MV411(human AML cell line), showed cytotoxicity ( $IC_{50}=184$  to  $218$  nM).<sup>30</sup>

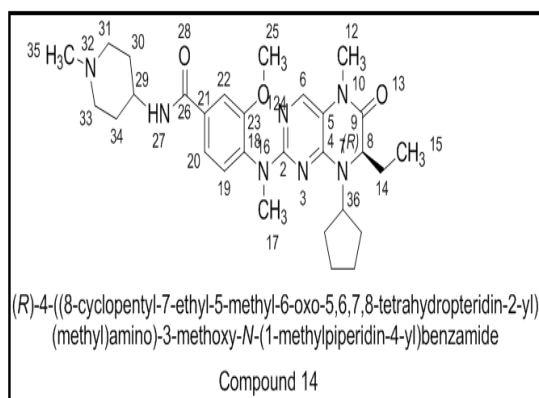


Fig. 39.

Sapkota *et al.*, reported ribosomal S6 kinases (RSK) inhibitors that have been linked to the development of cancer by being engaged in cell cycle progression and survival, Among the synthesized compound, Compound 17 (BI-D1870), By competing with ATP at the N terminal domain, it emerged as a particular selective inhibitor of the four RSK isoforms (about 99 percent inhibition observed at  $10\ \mu\text{M}$  concentration), supporting studies on RSK pathways in HEK293 and Rat-2 cells.<sup>31</sup>

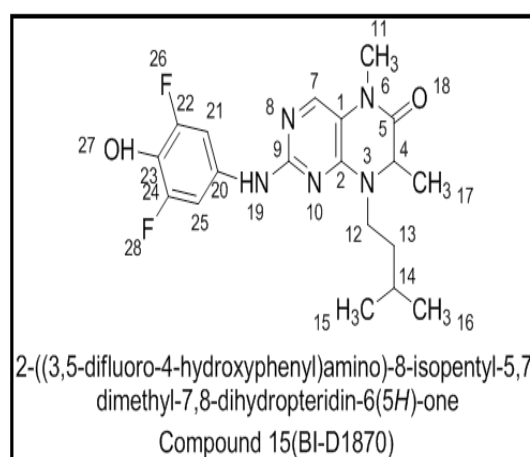


Fig. 40.

Mohammad KS *et al.*, reported and synthesized a series of TGF- $\beta$ -RI Kinase Inhibitors. Transforming growth factor shows tumor suppressive action on epithelial cells is; yet, when acting on cancer cells, this protein has been linked to tumor development and metastasis. TGF increases the kinase activity of TGF receptors I and II (TGFRI and TGFRII), SD208 (compound 16) was identified from the synthesized compounds as a TGFRI inhibitor ( $IC_{50}=0.048$  mol/L). A noticeable tumour growth and metastasis prevention observed when various xenograft mouse models treated with this synthesized derivative along with considerable immune cell infiltration.<sup>32</sup>

Song *et al.*, recently studied and reported a new and potent Transient receptor potential melastatin 7 kinase inhibitor, which has the ability to suppress breast cancer cell migration and invasion. Among the potential compounds, Inhibitory action of migration and invasion in breast cancer cells were found in prepared Compound 17, with  $IC_{50}=1.07\ \mu\text{M}$ . Wound healing and transwell invasion studies using MDAB468 breast cancer cells and TRex293 cells,

screened to this synthesized derivative revealed suppression of relocation and metastasis with minimal cytotoxicity.<sup>33</sup>

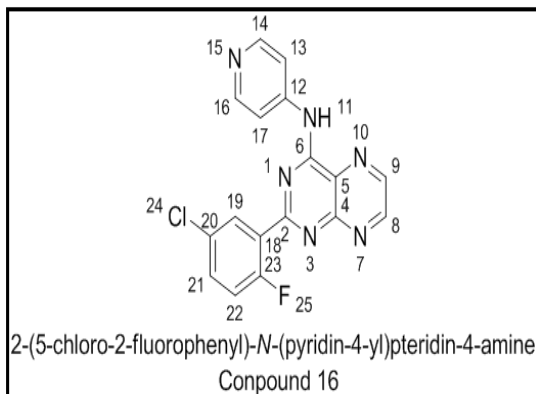


Fig. 41.

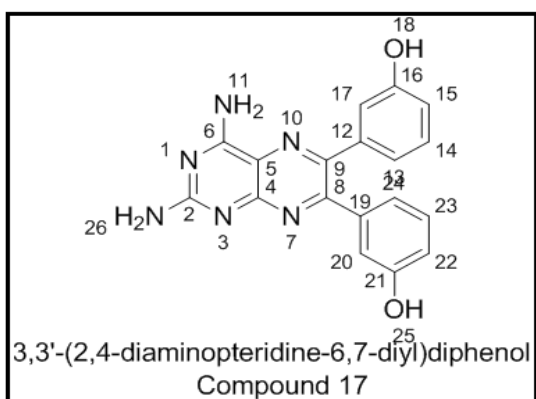


Fig. 42.

Xiaoyuan Li *et al.*, reported and synthesized derivatives of 5-substituted 2-amino-4-chloro-8-((4-methoxy-3,5-dimethylpyridin-2-yl)methyl)-7,8-dihydropteridin-6(5H)-ones derivatives as Hsp 90 inhibitor. The prepared Compound 20 was found as the most active and had the best selectivity for cancer cells among the prepared compounds. Results were observed: MCF-7,  $IC_{50}$ =50 nM, HT29  $IC_{50}$ =60nM, SKBR-3,  $IC_{50}$ =20nM, and BT474,  $IC_{50}$ =30nM.<sup>34</sup>

Su *et al.*, synthesized derivatives, which focused on kinases (Jak) are a family of nonreceptor tyrosine kinases that have been produced and tested. Auto phosphorylated Jaks, activates signal pathways, including STAT (STATs), resulting in cell proliferation and apoptotic arrest. This scaffold has derivatives, including synthesized compound 22,

with substituted pteridine ring. It inhibited Jak1 and Jak2 *In vitro* with  $IC_{50}$  values of 1.5 $\mu$ M and 0.8 $\mu$ M, respectively, along with the growth of BaF3 TEL-Jak2 cells with  $IC_{50}$ =0.53 $\mu$ M.<sup>35</sup>

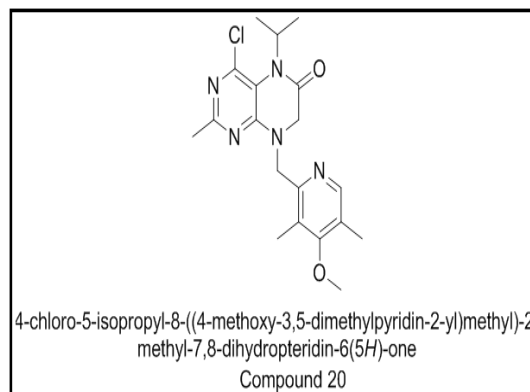


Fig. 43.

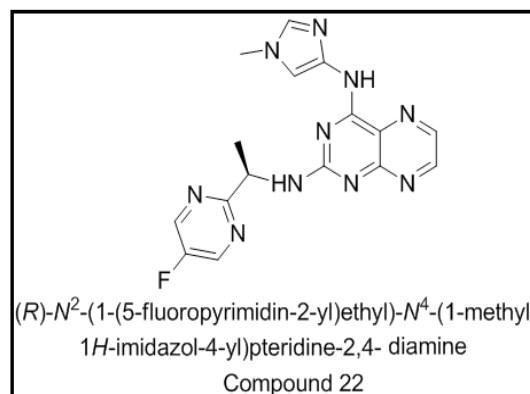


Fig. 44.

Murgueitio MS *et al.*, focused and synthesized Toll-like receptor 2 (TLR2) agonists and used them as dendritic cell (DC) vaccination adjuvants. DCs from the patient are extracted, activated *ex vivo* using TLR agonists and tumor antigens, and then reintroduced into the patient. Among the compounds in the series, Compound 23 was discovered to be an allosteric agonist and to be bound to the TLR1-TLR2 complex at distinct locations, with an  $IC_{50}$  of 5.26nM.<sup>36</sup>

Chauhan PM *et al.*, reported a dedicated 6,7-dimethylpteridine derivatives, with various heterocycles substituted at position 2 that were coupled to thioether or alkylamino in position 4. Some of these synthesized and analyzed derivatives, including compound 24, have demonstrated

cytotoxicity against cancer cell lines MCF7 (breast), NCIH460 (lung), and SF268 (center-neuronal system) of 0.1  $\mu\text{M}$ , however the largest inhibitory impact on cell development was not less than 57 percent.<sup>37</sup>

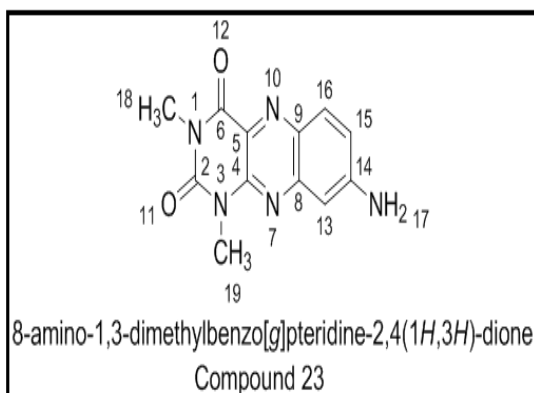


Fig. 45.

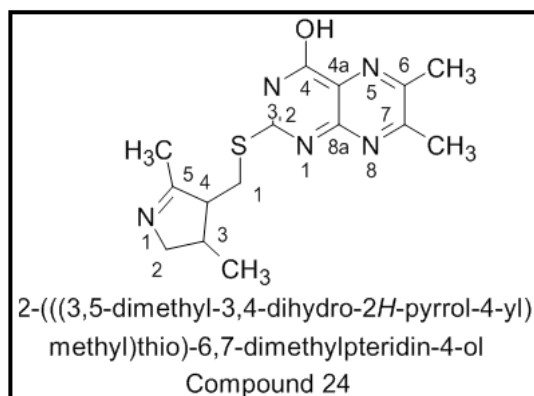


Fig. 46.

Geng PF *et al.*, reported A new class of 5,8-dihydropteridine-6,7-diones tested on number of cancer cell lines. From the derivatives analysed, those with a piperazine substitution produced the best outcomes, including cell lines like, MGC-803 and SGC7901 (gastric cancer), A549 (lung), PC3 (prostate cancer) (prostate) cell lines. Compound 25 proved to be the most potent anticancer drug, with  $\text{IC}_{50}$  values of less than 20  $\mu\text{M}$  for each cell line examined. In a wound-healing experiment, this medication also decreased MGC-803 (indirect neoplastic transformation measurement) cell production and migration. Furthermore, compound 25 emerged with an attractive result with an SI of 4.36 between MGC803 and normal gastric epithelial cells.<sup>38</sup>

Li ZH *et al.*, reported pteridine-7(8H)-one

derivative, MKN45 and MGC803 (gastric cancer), H1650 (lung cancer), and EC109 cell lines were tested (esophagus cancer). Compound 26 has  $\text{IC}_{50}$  values of less than 10  $\mu\text{M}$  in each case within the tested series. Further research showed that apoptosis was induced, as evidenced by a propidium iodide (annexin V) experiment and validation is observed by increment in Bax expression and lower levels of Bcl-2, caspase-3, and 9 cleavages.<sup>39</sup>

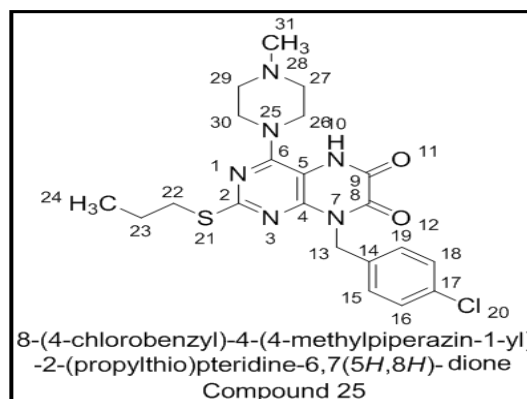


Fig. 47.

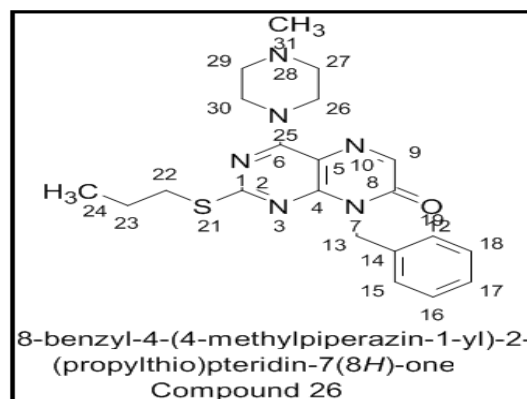


Fig. 48.

Novosad D *et al.*, reported a novel 6-azapteridines via a cyclocondensation reaction from the corresponding aryliminohydrazones. Compounds 27a and 27b were identified as the potent derivatives. In particular, when examined in several cancer cells like MCF7 and K562, 27a had  $\text{IC}_{50}$  values of 8.3 and 12.9  $\mu\text{mol/L}$ , respectively, whereas 27b had  $\text{IC}_{50}$  values of 7.2 and 14.6  $\mu\text{mol/L}$ .<sup>40</sup>

Miyoshi T *et al.*, synthesized derivatives from which, two M2-(N, N-dimethyl-aminomethyl-eneamino)-3-pivaloylpteridin-4-ones

derivatives, From the synthesized compounds, Compounds 28 a and 28 b, screened with Panic-1 cancer cell line, The dosages of prepared derivatives were adjusted from 2mM

(28 a) to 400  $\mu$ M (28 b) reduced cell viability and exacerbated cell apoptosis caused by UVA irradiation. The findings also demonstrated that 28 a induced G2/Marrest.<sup>41</sup>

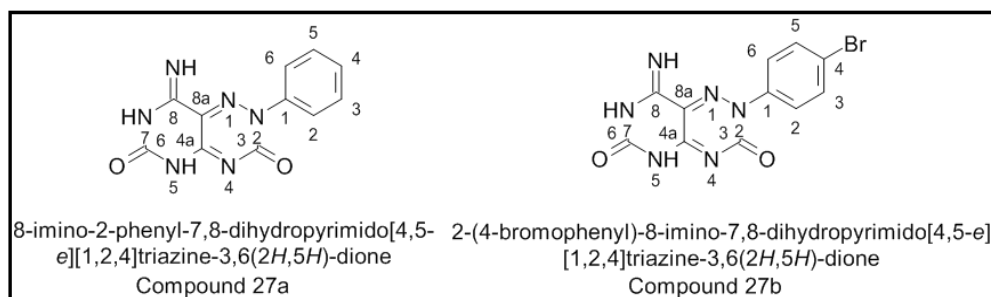


Fig. 49.

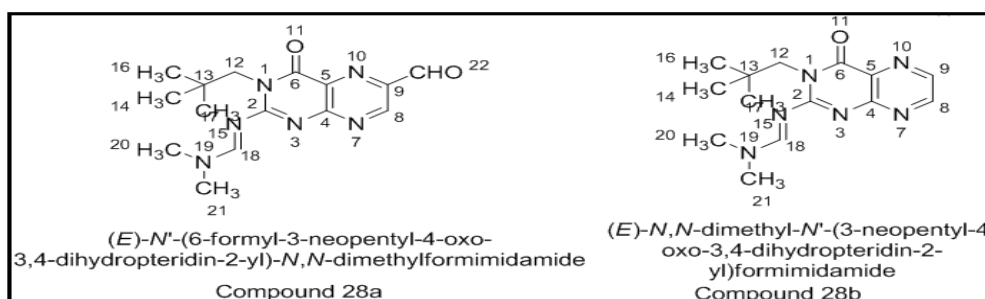


Fig. 50.

## CONCLUSION

By evaluating the distinctive pteridine derivatives, it's evident that this heterocycle incorporates a big selection of potential as a growth agent. Pteridine, with its effective action and skill to act with different heterocycles, might without delay be utilized to create a range of neoplastic derivatives. Pteridine derivatives have additionally been shown to be effective malignant neoplasm agents, and these promising synthesized derivatives of the heterocycle have the power to influence a good range of cell lines, indicating that they may be helpful and versatile anticancer agents. It takes heaps less effort to make a scaffold that

meets all of the standards for an ideal malignant neoplasm drug.

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## Conflicts of interest

We state unequivocally that we do not have any conflicts of interest.

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