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SCHIFF BASE: A REVIEW OF PHARMACOLOGICAL ACTIVITIES

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Keywords:

Schiff base, Antimicrobial, Pandemic, Therapeutic

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ABSTRACT: Schiff bases are generally aldehyde or ketone-like compounds in which an imine or azomethine group replaces the carbonyl group. They are versatile and exhibit a broad range of pharmacological activities as antimicrobial, antibacterial, antifungal, antiviral, and anticonvulsant. Anti-cancer activity has been used widely for industrial purposes or therapeutic use. Thus, Schiff bases are highly desired environment-friendly organic compounds used for various therapeutic activities. The goal of reviewing all therapeutic properties is to enhance and modify the antimicrobial properties of the Schiff base. Due to the pandemic conditions of the past few years, it is now necessary to have a compound with strong antimicrobial properties to fight any microorganisms.

INTRODUCTION: Schiff base **Fig. 1** and their complexes are versatile compounds, synthesized from the condensation of an amino compound with carbonyl compounds and widely used for industrial purposes due to their easy formation and rich coordination chemistry with a large variety of metal ions, including antifungal, antibacterial, antimalarial, antiproliferative, anti-inflammatory, antiviral and antipyretic properties [1-9].

Nobel prize winner HUGO SCHIFF firstly introduced Schiff bases in 1869. Structurally, a Schiff base which is (also known as imine or azomethine) is a nitrogen analogue of an aldehyde or ketone in which carbonyl group(c=o) is replaced by the imine or azomethine group **Fig. 2** [10].

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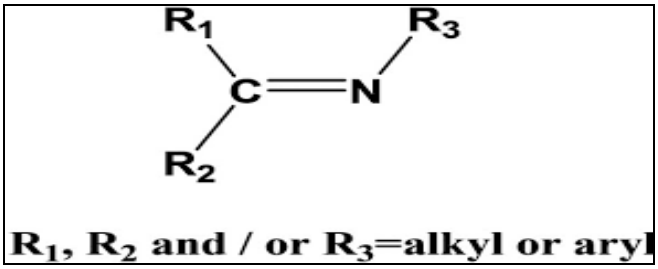


FIG. 1: STRUCTURE OF SCHIFF BASE

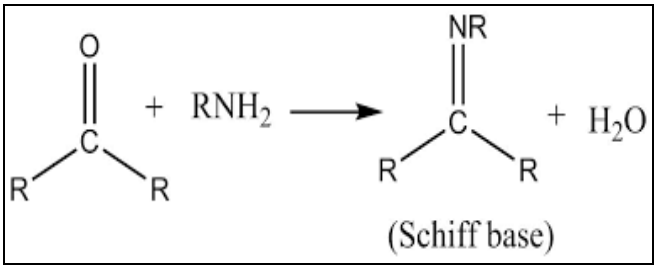
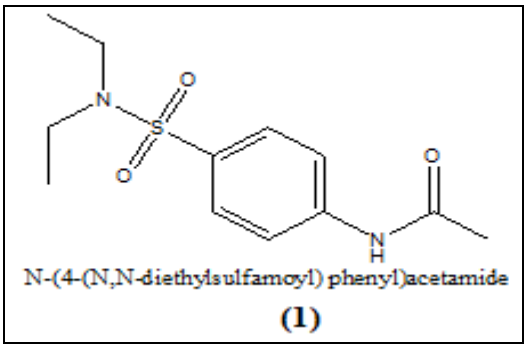


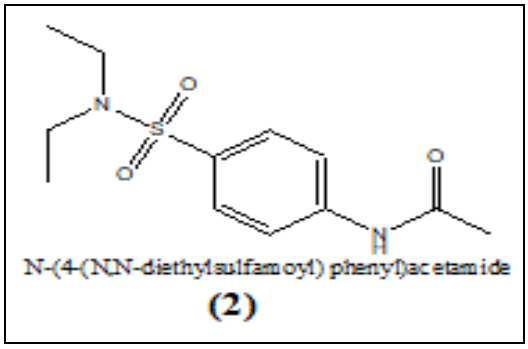
FIG. 2: SCHIFF BASE REACTION

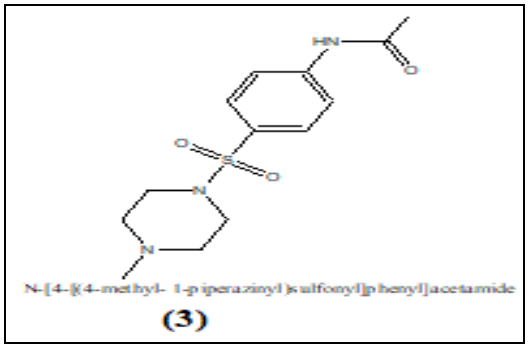
1. Biological Importance of Schiff Base:

1.1 Analgesic Activity: As sulphonamides are good antimicrobial in nature, researchers synthesized a new series of N-phenylacetamide sulphonamides, and in this series N-[4-[(4-methyl-1-piperazinyl) sulfonyl] phenyl] acetamide(1)

exhibited good analgesic activity which is more potent than any other previous compound, while the compounds N-(4-(N, N-diethylsulfamoyl) phenyl) acetamide (2**)** and N-(4-(piperazin-1-ylsulfonyl) phenyl) acetamide (3) showed an important anti-hypernociceptive activity which is good in inflammatory pain [11].

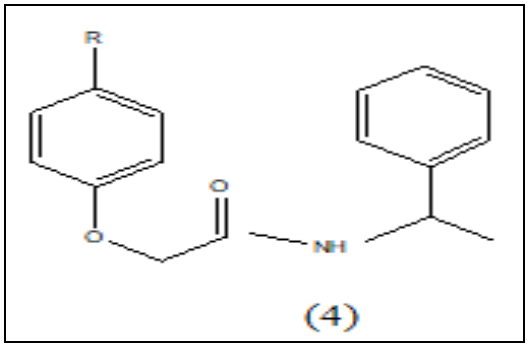




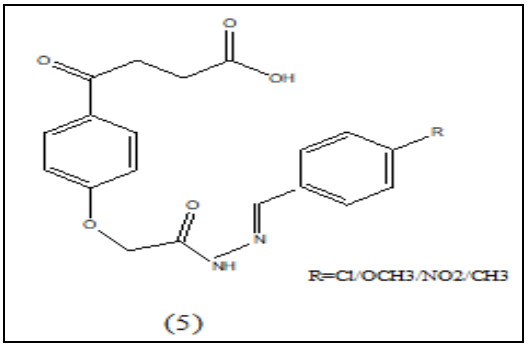


The synthesized compound N-(acridine-9-yl)-4. benzo (d) imidazole loxazole-2-yl) benzamides revealed that schiff bases exhibit good analgesic and anti-inflammatory activity [12].

2.2 Anti-inflammatory Activity: When a novel series of 2-(substituted Phenoxy)-N-(1-phenylethyl) acetamide (4) is synthesized with the help of a reaction between 1-phenylethylamine and substituted phenols, the result indicates that halogen-containing Phenoxy derivatives of Schiff base enhanced the anti-inflammatory activity and the derivatives contain nitro group exhibited good anti-cancer, anti-inflammatory and analgesic activities [13].

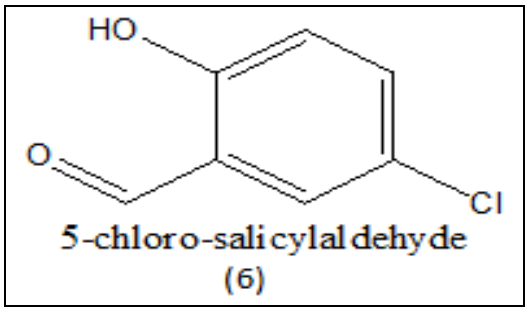


A new series of Phenoxy acid hydrazides (5) derivatives illustrated anti-nocieptive and anti-inflammatory activity, because of the acidic moiety, which enhanced the peripheral action of anti-nociception and decreased the central activity of anti-nociception [14].



1.3 Antimicrobial Activity: The synthesized novel series of Schiff bases derived from the condensation of 5-chloro-salicylaldehyde (6) & primary amines showed that the derivatives were most active against the standard bacterial species. It has also been reported that the efficiency of the Schiff bases in inhibiting the growth of fungi such as *A. fumigates*, *A. flavus*, *Trichophyton*

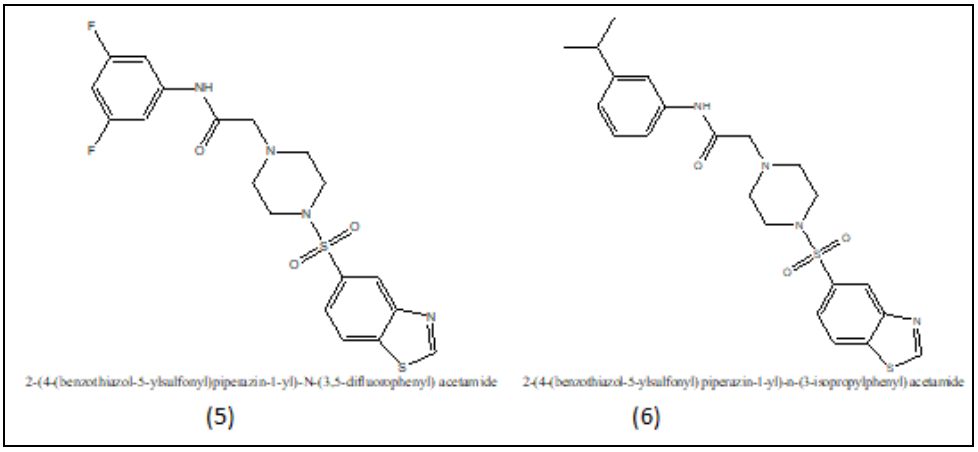
mentagrophytes and *Penicillium marneffei* was noticeably good [15].

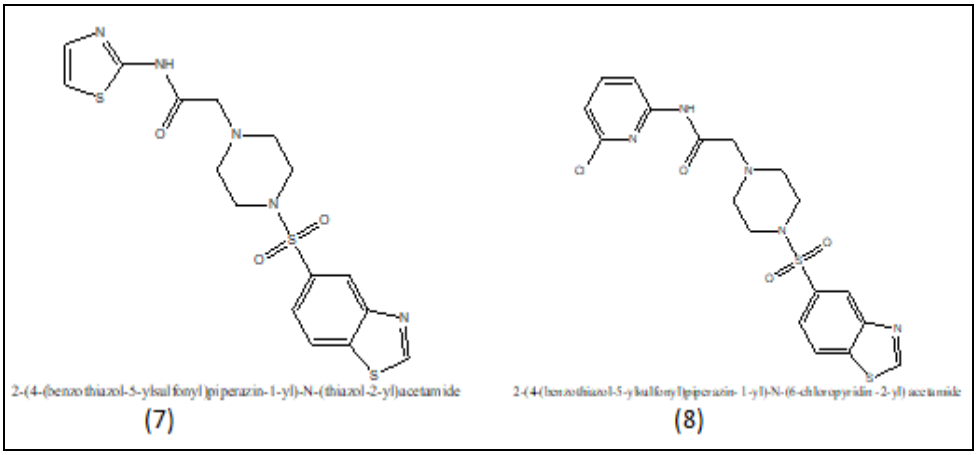


1.4 Antioxidant Activity: Likewise, series of Co(II), Ni(II), Cu(II), Cd(II), Zn(II) and Hg(II) complexes of neutral bidentate Schiff base with azomethine nitrogen and carbonyl oxygen donor atoms , the resulted derivatives showed varying antioxidant activities while Ni(II), Zn(II) and Hg(II) complexes have exhibited good antioxidant activity. Further, the DPPH (2, 2-diphenyl-1-picrylhydrazyl) scavenging capacity of the synthesized compounds depends on the concentration [16].

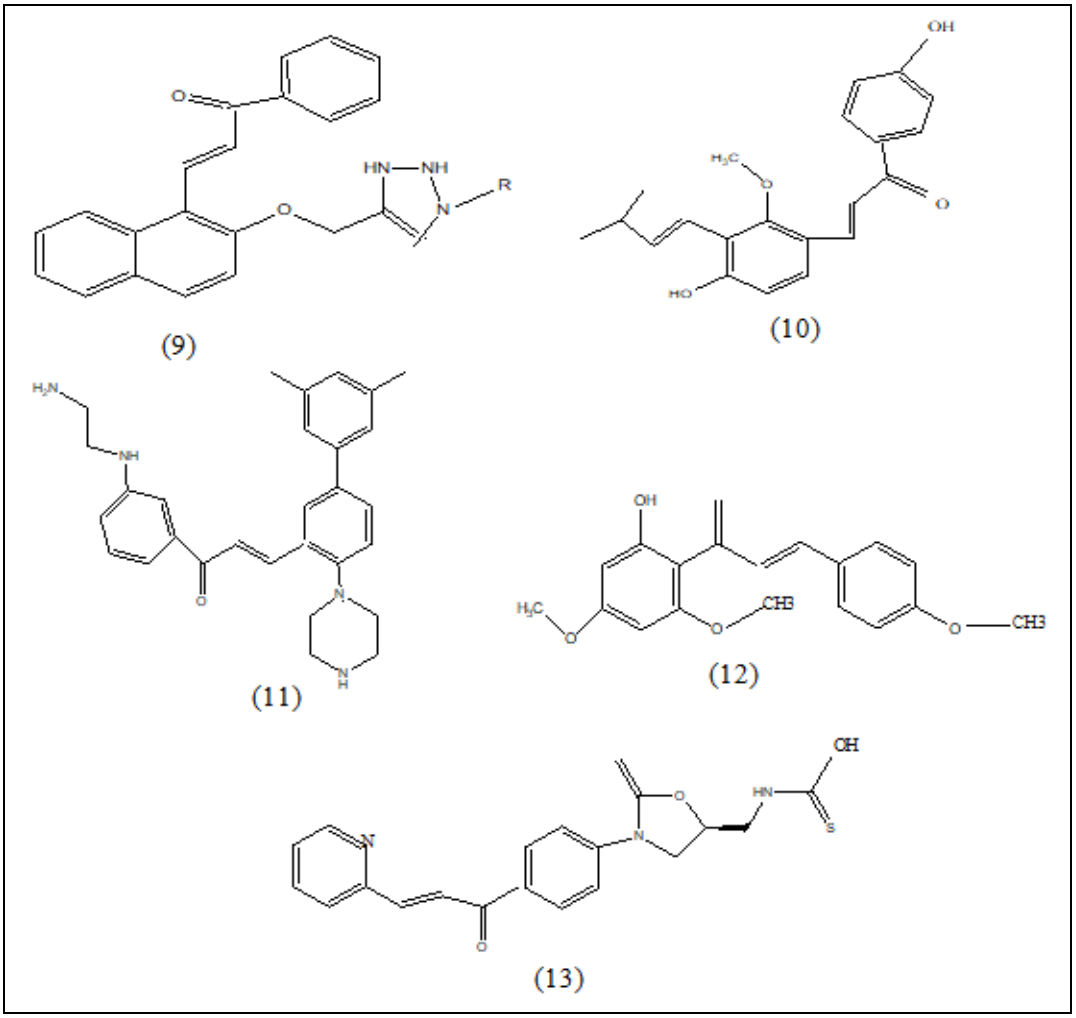
1.5 Antibacterial and Antifungal Activity: All synthesized derivatives of acetamide compounds *e,g.*

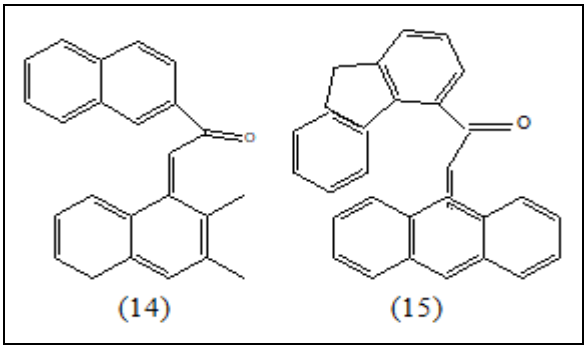
- 2-(4-(benzothiazol-5-ylsulfonyl) piperazin-1-yl)-N-(3,5-difluorophenyl) acetamide (5) and
- 2-(4-(benzodthiazol-5-ylsulfonyl) piperazin-1-yl)-N-(3-isopropylphenyl) acetamide were illustrated good activity against gram-positive bacteria as according to litreture survey.
- Another two acetamide compounds 2-(4-(benzothiazol-5-ylsulfonyl)piperazin-1-yl)-N-(thiazol-2-yl)acetamide and
- 2-(4-(benzothiazol-5-ylsulfonyl) piperazin- 1-yl)-N-(6-chloropyridin -2-yl) acetamide were exhibits good activity against fungi [17].



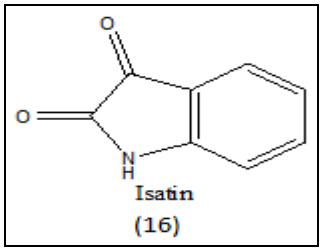


As the result of anti-biotic resistance and other factors the researchers are looking for new active compounds against multidrug-resistance pathogens and screamed compounds (9-15) positively which displayed very good results [18].

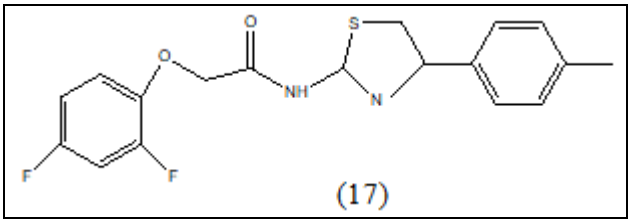




Schiff bases containing 2, 4-dichloro-5-fluorophenyl exhibited good antibacterial activity by effectively inhibiting bacterial growth. Schiff bases derivatives derived from isatin (16) showed excellent anti-HIV and antibacterial activity [19-20].

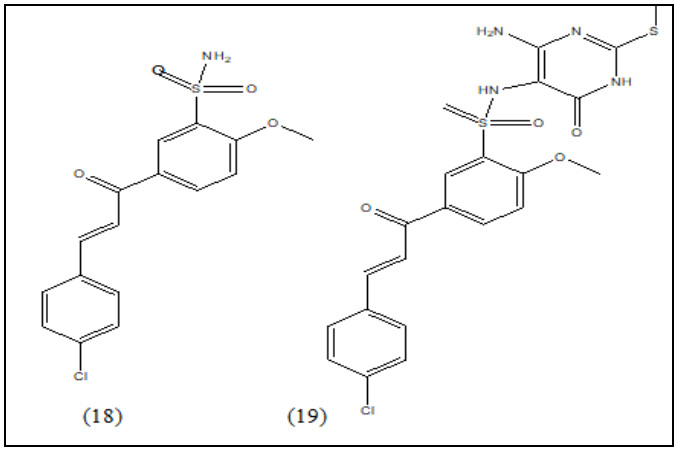


1.6 Anticancer Properties: Likewise, in 2018, a novel series of Phenoxy thiazoles were synthesized. The result revealed that the compound (17) with methyl and fluoro substitute has potential cytotoxic efficacy with an average IC_{50} value of~ 13 µM. The potent compounds were further analyzed for anti-tumor studies that showed a significant role against the tumor cells by repressing HIF-1α by p53/MDM-2 mediated degradation. The experimental result favored the compound with good cytotoxic efficacy with prolonged activity against different cancer cell lines and against Dalton's solid lymphoma progression [21-22].



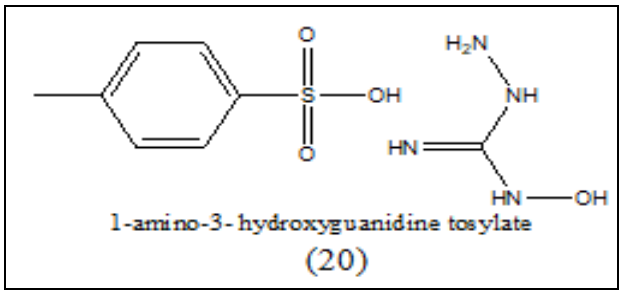
The researchers synthesized two new series of compounds (E)-5-(3-(4-chlorophenyl) acryloyl)-2-

methoxybenzene- sulfonamide (18) and (E)-N-(4-amino – 2 - (methylthio) – 6 - oxo-1, 6-dihydropyrimidin – 5 - yl) – 5 - (3 -(4-chlorophenyl) acryloyl)-2 methoxy benze-nesulfonamide (19) were exhibited potent anti-cancer activity against the majority of cell lines, especially HCT-116 for compound (18) and SF539 for (19) compound [26].



1.7 Antiviral Properties: Schiff bases itself play a vital role as antiviral and derivatives derived from isatin and bisisatin exhibited good activities against different strains of viruses. Schiff bases derived from prodrug abacavir (Ziagen) were reported as anti-HIV agents, and Schiff bases of 2-phenylquinazoline-4(3)H-one were reported to show antiviral activity against the strains of viruses like feline coronavirus, influenza viruses, and herpes simplex virus according to literature survey [27-29].

Myricetin derivatives of schiff base containing 1,2,4-triazole, were designed and synthesized, Which exhibit a good inhibitory effect against Xanthomonas axonopodis pv. Citri (Xac), respectively, were better than bismerthiazol and thiodiazole copper [30]. Salicylaldehyde Schiff bases derived from 1-amino-3- hydroxyguanidine tosylate (20) act as new antiviral agents [31].



A series of 3-(benzylideneamino)-2-phenylquinazoline-4(3H)-one, 3(a–l) **Fig. 3** was synthesized and analyzed for cytotoxicity and antiviral activity, in which Compounds having 2-hydroxy substitution showed better antiviral activity [40].

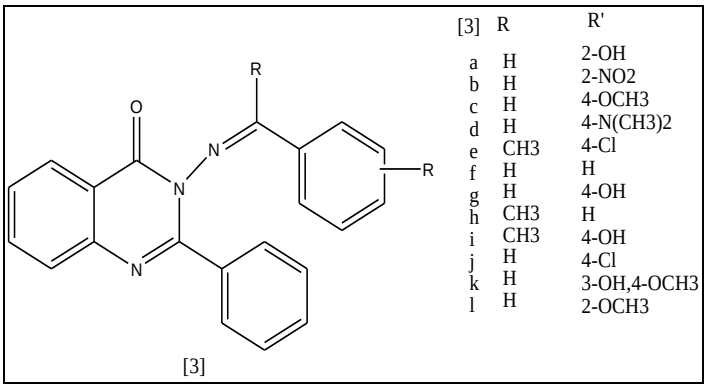
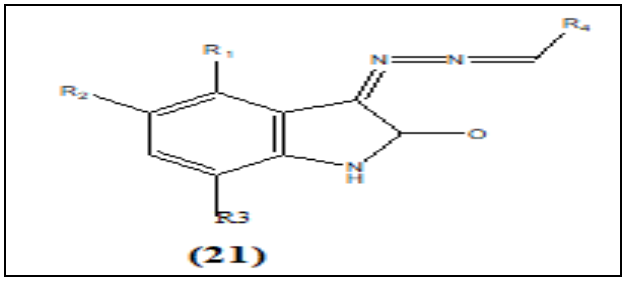
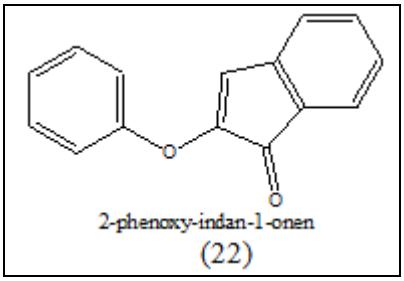


FIG. 3:

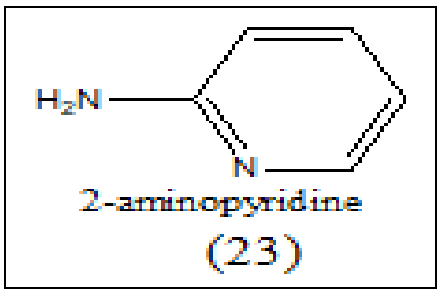
1.8 Anti-glycation Activity: A new derivative of bis-Schiff bases was synthesized and evaluated the *in-vitro* anti-glycation potential, and compounds (21) showed excellent anti-glycation activity. The para- and ortho-nitro analogues were found to be as most active agents. They were also reported as the dihydroxy analogue was found as the third most active anti-glycating agent [32].



1.9 ACE Inhibitor Activity: A novel derivative Schiff base *e.g* 2-phenoxy-indan-1-ones (22**)** has been synthesized, showing that most of the compounds exhibited high activity of AChE inhibition, while all the compounds were almost inactive against BChE [33].



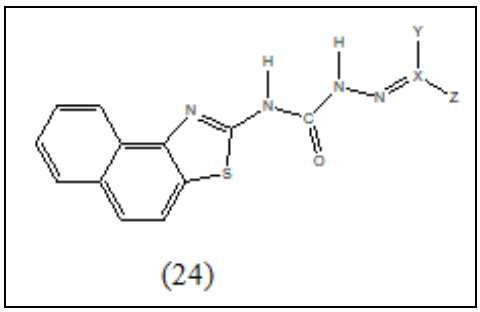
1.10 Anticonvulsant Activity: A novel series of new Schiff bases of 2-aminopyridine (23) were synthesized and illustrated as these Schiff bases show better anticonvulsant potency against MES and Sc.-PTZ [33].



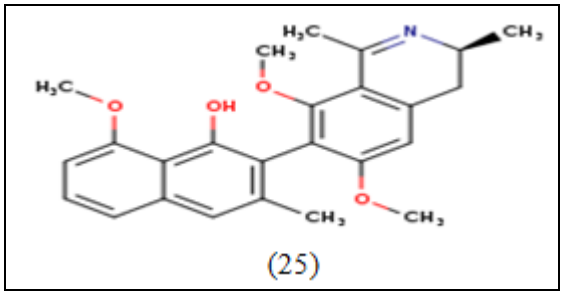
2-Aminopyridine derivatives have been detected for lipid absorption inhibitors [34]. Substituted benzyl pyridines are good for preventing convulsions. In past years few amino-pyridine derivatives are known as sodium channel modulators with many therapeutic applications, especially in the treatment of convulsions, depression, and pain [35].

Some novel 3-aryl-4(3H)-quinazolinones- 2-carbo-xaldehydes and other derivatives of Schiff's bases showed anticonvulsant, analgesic, and cytotoxic drug potential activity due to thiosemicarbazone side chain [36].

A novel series of N4-(naphtha [1, 2-d] thiazol-2-yl) semi-carbazides (24) synthesized for the investigation search for novel antiepileptic drugs with neuroprotective properties [37].



1.11 Anti-malarial Properties: Human malaria is largely caused by four species of the genus Plasmodium (*P. falciparum, P. vivax, P. ovale,* and *P. malariae*). Schiff bases are versatile compounds and efficient moiety for antimalarial drugs. For example, the compound with such effect is Ancistrocladidine [25]. Ancistrocladaceae and Dioncophyllaceae and presenting an imine group in a molecular chain [38].



Ancistrocladidine – the antimalarial activity of bioactive Schiff base. The literature survey revealed that the synthesized simple Schiff base,N-(pyridine-4-methlene) quinuclidine-3-amine,from 3-mino-quinuclidine and 4-pyridine carbo-xaldehyde exhibits physiochemical properties were shows the result that these compounds exhibited very good efficiency against malaria viruses due to the ligand-protein responsible for the inhibitory potency [39].

CONCLUSION: The above literature review demonstrates that Schiff-base exhibited versatile pharmacological activity, especially antimicrobial effects against various microorganisms. Structure-activity relationship of Schiff-base-containing derivatives indicated that Schiff-base moiety is essential for pharmacological activity as antimicrobial, antibacterial, antimalarial, anti-convulsion, anti-glycation, and antiviral activity. It has already been used for therapeutic as well as industrial purposes widely. Schiff bases explored its biological activity efficiently, but their compound needs further investigations to be promising leads for the design of a more efficient antimicrobial agent. Because of its high efficacy and lower side effect, this ring may be positively useful for these pandemic-related conditions.

DECLARATION:

Ethical Approval and Consent to Participate: Not applicable

Consent for Publication: Not applicable

Availability of Data and Materials: The data presented in the study are included in the article and supplementary information.

Author's Contribution: The author drafted the manuscript and wrote most of the article. The co-authors participated in the discussion and helped to write the manuscript.

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CONFLICTS OF INTEREST: There is no competing interest

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