PROJECTREPORT

On

SYNTHESISOFQUERCETINBASEDSCHIFFBASEANDITS ANTI-INFLAMMATORY ACTIVITIES

Submitted by
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Inpartialfulfillmentfortheawardofthe Post graduate Degree in Chemistry

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M.Sc.CHEMISTRYPROJECTREPORT

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CERTIFICATE

This is to certify that the project work titled "**SYNTHESIS OF QUERCETIN BASEDSCHIFFBASEANDITSANTI-INFLAMMATORYACTIVITIES**"is the work done by **JAYALAKSHMI J.** and **SONA MARY MARTIN** under the guidance of **Dr. ShantyA. A. AssistantProfessor** Department of Chemistry and Centre for Research, St. Teresa's College, Ernakulam in partial fulfilment of the awardofthe Degree of Master of Science in Chemistry at St. Teresa's College, Ernakulam affiliated to Mahatma Gandhi University, Kottayam.

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ProjectGuide

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CERTIFICATE

Thisistocertifythattheprojectworkentitled"**SYNTHESISOF QUERCETINBASEDSCHIFFBASEANDITSANTI-INFLAMMATORY ACTIVITIES**"istheworkdonebyJAYALAKSHMIJ.and**SONAMARY MARTIN** under my guidance in the partial fulfilment of the award of the DegreeofBachelorofScience in Chemistry at St. Teresa's College (Autonomous),ErnakulamaffiliatedtoMahatma Gandhi University, Kottayam.

Dr.ShantyA.A.
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DECLARATION

Iherebydeclarethattheprojectwork entitled "**SYNTHESIS OF QUERCETINBASEDSCHIFFBASEANDITSANTI-INFLAMMATORY ACTIVITIES**"submittedtoDepartmentofChemistryandCentrefor Research, St. Teresa's College (Autonomous)affiliatedtoMahatma Gandhi University, Kottayam, Kerala is a record ofan original work done bymeundertheguidanceof**Dr. ShantyA. A. AssistantProfessor,** Department of Chemistry and Centre for Research, St. Teresa's College (Autonomous),Ernakulam.This project work is submitted in the partial fulfillment of the requirements for the award of theDegree of Master of Science in Chemistry.

JAYALAKHMI J.
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Contents

Chapter 1

Introduction

1.1 SCHIFFBASE

The discovery of new chemotherapeutics with novel bioactivities and functionalities to fight current emerging diseases has become the most significant researchinpharmaceuticalsscience.Schiffbasesareadaptable pharmacophores that can chelate with metals in a variety of oxidation states to produce complexes. The discovery of new chemotherapeutics with novel bioactivities and functionalities to fight current emerging diseases has become the most significant research in pharmaceuticals science.

Schiff base are the complexes synthesized from the condensation of primary amines with carbonyl groups which are used in various fields (Figure1.1). Hugo Schiff originally wrote about them in 1864.Schiff base are versatile C=N (imine) containing compounds having broad spectrumof biological activities. And they also showed some degree ofantibacterial, anti-inflammatory activities. Mainly Schiff base are used as intermediates for the synthesis ofamino acids and also used asligands for the preparation of metal complexes[1].

Figure1.1: GeneralSchemeofformationofSchiffBase

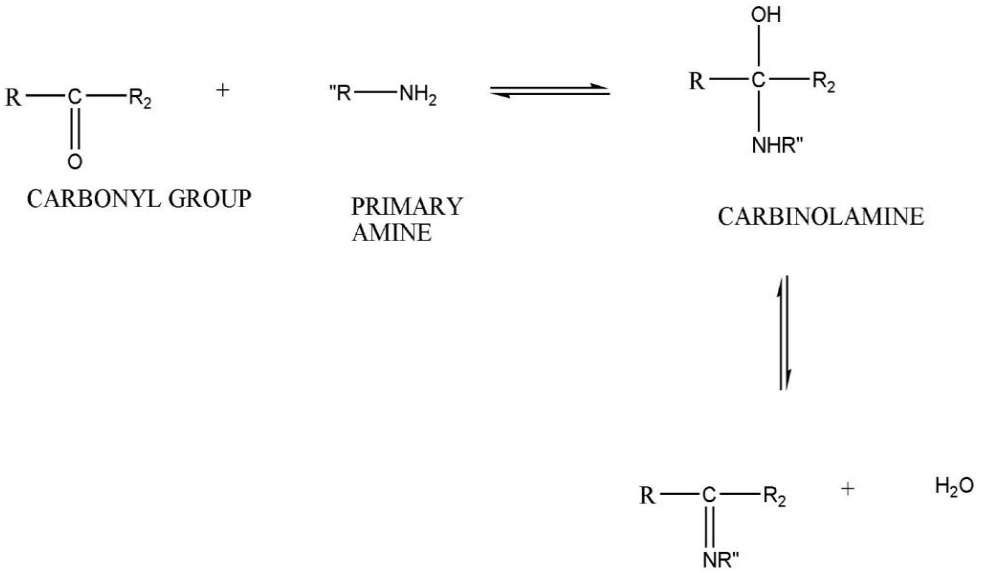


Figure1.2:MechanismshowingtheformationofSchiffBase

Aldehyde or Ketone combineswithprimaryamine to give carbinolamine where the double bond between C and O gets broken and leads to the formationofanOH bond. The alcoholic group Carbinolamine which is an unstableadditioncompoundundergoesacidorbase catalyzeddehydration. Following the removal of water, Carbinolamine gives an Imine with C=N bond (Figure1.2). The reaction of forming Imine is a reversible reaction. Addition followed by elimination are the two types of reaction that taking place in the formation of Schiff Base [2].

Theazomethinegroup,whichissharedbySchiffBasecompounds,hasthe generic formula RHC=NR1, where R and R1 are heterocyclic, cycloalkyl, or aryl groups that can be substituted in many ways. These substances are also known as imines, or azomethines. Arylsubstituted Schiff bases are more stable compared with alkyl substituted because of its alternative doublebonds.Researchhasshownthatthepresenceofasinglepairof

electrons in the nitrogen atom's SP^2hybridized orbital of the azomethine group has important chemical and biological ramifications. Because of their special C=N group trait, synthetic flexibility, and relative ease of synthesis, schiff bases are often excellent chelating agents. The versatility of Schiff base ligands and the uses of their complexes in biology, chemistry, and industry make more research in this field extremely desirable [3].

The most Important research in pharmaceutical science today is the development of innovative chemotherapeutics with unique bioactivities and functionality to combat newly emerging diseases. Because of their numerous and valuable scientific applications, Schiff base metal complexes have been the focus of coordination chemistry research during the course of several decades of rigorous study on metal-based pharmaceuticals. They may be used as antibacterial, antimicrobial, anticancer, antiviral, anti-inflammatory, analgesic, antifungal, and many other medicinal medicines.

Medicinal resistance has become a global problem in medical research in recent years due to the majority of pathogenic organisms being able to deactivate medicinal compounds. For this reason, it Requires urgent attention from chemical and pharmaceutical scientists to address thesevere challenges of multidrug resistance [4].

1.2 BIOLOGICALAPPLICATIONSOFSCHIFFBASE

A carbonyl group and an amino group condense to form Schiff Base ligands and their complexes.The resulting metal complexes may possess antioxidant, antifungal, and antibacterial qualities[5]. In many enzymatic processeswhereanenzymeinteractswithanaminoorcarbonylgroupof

the substrate, Schiff Base appears to be a crucial intermediary. In organic chemistry, it has severalsynthetic applicationsas well.AcylationofSchiff Bases by acid anhydride, acid chlorides and acyl cyanides is initiated by the attack on the nitrogen atom and it leads to the net addition of the acylation agent to the CN double bond. These exhibit substantial antibacterial action as well. The metalcomplexes ofthe Schiff Bases have muchbetterantibacterialactivitythantheir free ligands [6]. Forimproving the product yield Schiff Base metal complexes can be used which have strong catalyst activity. For the peroxidation of several alkenes including cyclohexene, cis and trans stilbene, cyclooctene, the complexes ofV, Mn, Fe, Co, Cu and Zn ions were utilized as catalysts [7].

1.2.1 ANTIDEPPRESENTACTIVITY

Schiff bases of isonicotinoyl hydrazone N-[(1Z)-sustituted aromatic)methylidene] pyridine-4carbo hydrazides werefoundtohave considerable antidepressant and nootropic properties in vitro. Compounds substituted with nitro, halogen, and dimethoxy groups also had strong antidepressant properties [8].

1.2.2 ANTIMALARIAL ACTIVITY

The malaria genus is caused by Plasmodium. In general, Plasmodium is made up of four species. P. Vivax, P. Falciparum, P. Ovale, and P. Malaria. Serious health issues could result from malaria.Nowadays, the hunt for novel medications to treat this illness is essential. Antimalarial medications can be made from Schiff bases. N-[(1E)-(5-nitro-1-naphthyl)methylene]-1-(2-(tri-fluoromethyl)phenyl]methanaminewasthe

most effectiveantimalarial agent among 5 nitroisoquinoline Schiff bases[9].

1.2.3 ANTIINFLAMMATORYACTIVITY

One of the body's main defense mechanisms against infection, poisonous substances, allergies, and other unpleasant stimuli is inflammation[9]. In manychronic conditions, anunchecked and ongoing inflammation maybe a contributing cause [4]. Additionally, medicines with Anti Inflammatory properties are imidazole groups that contain Schiff base transition metal complexes.

Conversely, diseases caused bymicroorganisms, suchas bacteria or fungi, are typically benign and increase gradually in fatality [10]. NSAIDs and analgesics, which are often used Anti Inflammatory medicines, have been linked to a number of side effects, including myocardial infarction [11], congestive heart failure, nausea and vomiting, dyspepsia, stomach ulceration/bleeding, diarrhea [12], hypertension, and retention of salt and fluids. Numerous biological effects, including those that are anti-inflammatory, analgesic, antiviral, antipyretic, antirheumatic, and antibacterial, have been demonstrated by the pyrazolone derivative 4aminoantipyrine (4-amino-1,5-dimethyl2phenylpyrazole-3-one) and its derivatives. Mohammad Sayad Alam, Jung-Hyun Choi,Dong-Ung Lee conducted experiments on this derivative. These groupsofsubstances also function as potent inhibitors of the synthesis of prostanoid, platelet thromboxane, and cycloxygenase isoenzymes [13].

1.2.4 ANTIOXIDANTACTIVITY

Antioxidants are naturally occurring chemicals that protect living organisms fromdamage caused by harmful molecules called free radicals. These are produced by her cells in the body in response to free radicals [14].Freeradicals play an important role in the pathogenesis of many diseases, including cancer, diabetes, liver damage, autoimmune diseases, heart disease, atherosclerosis, and aging [15].Therefore, antioxidants with the potential to scavenge free radicals play an important role in the treatment and prevention of these diseases [16]. Antioxidants are often used as catalysts for antibiotics. Antioxidant compounds have a high ability to scavenge free radicals. Antioxidants play an important role in retardingorpreventingtheoxidationofoxidizablesubstances(substrates) [17],[18].Invivo,antioxidantcompounds prevent damage to 4,444 macromolecules and cells by interfering with free radical molecules [19]. Therefore, the importance of searching for antioxidants has increased dramatically in recent years [20].Currently, synthetic antioxidants are widely used as they are cheap and effective compared to natural anti oxidant [21].

1.2.5 ANTICANCERACTIVITY

By condensing salicyaldehyde with 2-amino-4-phenyl-5-methyl thiazole, a Schiff base ligand was created. In good yield, the ligand forms compounds with Zn(II), Cu(II), Ni(II),andCo(II).Elements analysis, magnetic susceptibility, molar conductance, infrared spectra, 1H and 13C NMR, mass, electronic absorption, and ESR spectroscopy were used to describe the produced compounds. In order to compare the anticancer activityofthesynthesizedcompoundswiththatofdoxorubicinasa

reference medication, the compounds' anticancer activity was investigated against many human tumor cell lines, including breast cancer MCF-7,livercancerHepG2, lungcarcinomaA549,andcolorectalcancerHCT116. In comparison to the inhibition in the four cell lines (HepG2, MCF7,A549, and HCT116), the study demonstrated that Zn(II) complexexhibited potent inhibitionagainst humanTRK by the ratios of 80, 70, 61, and 64%, respectively[22].

1.3 IMPORTANCEOFREAGENTSUSED

1.3.1 QUERCETIN

Family of secondary plant chemicals known as polyphenols is composed of rings of phenolic compounds. Polyphenols are known to be present in plant-based diets. They are typically found in plant-based products liketea, coffee, red wine, and chocolate in addition to a variety of fruits and vegetables. Recent research has demonstrated the preventive role of plant polyphenols against cancer, cardiovascular disease, and neurological illnesses. They are strong antioxidants that guard against oxidative damage. These polyphenols are secondary metabolites of plants and are essential parts of defense mechanisms in plants [23].

"Quercetin"istheLatinnamefortheflavonoid,andit means"oakforest." The human body does not manufacture this kind of flavonol.The benefits of quercetin for ailments like arthritis, cancer, allergic responses, inflammation, and cardiovascular disease have long been established. Moreover, mitochondrial biogenesis, platelet aggregation, and lipid peroxidation all depend on flavonoids [20]. A vast array of seeds, nuts, flowers, bark, and leaves can be found in nature. It is found in plants that arerelatedtotomatoes,canola,berries,onions,leeks,grapes,apples,and

tea [24]. In addition to ginkgo biloba, hypericum perforatum, and elderberries, the primary sources of quercetin are onions, apples, and tea [24]. The formula for it is $C_{15}H_{10}O_7$.

The polar auxintransport inhibitor is a naturallyoccurring substance.The oxygen atomon the first carbon ofthe quercetin molecule is basic and can react with strong acids to form salts. The molecule also contains a ketocarbonyl group.Its molecular structure consists of four active groups: an o-dihydroxy group (B), an inter-ring dihydroxy group (A),adouble bond(C2),aC3ring,anda4-carbonylgroup.Quercetinhas strong antioxidant qualities since it has phenolic hydroxyl groups and double bonds. Furthermore,studies carried out in vitro and in vivo have shown quercetin's antibacterial activity in addition to its effective suppression of related gene expression, anticancer activity, antiangiogenic activity, and other processes that aid in the formation of biofilms.Additionally, quercetin plays a major role in loweringmycotoxins, which protect cells from damage.

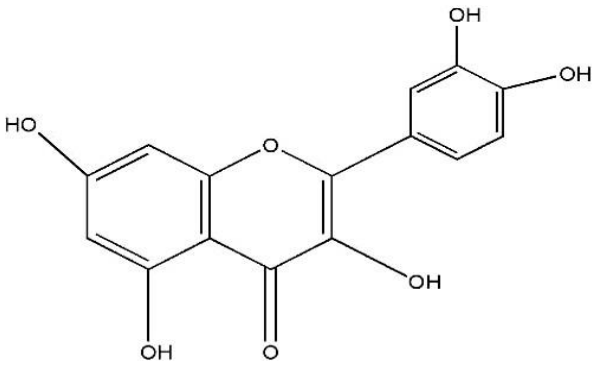


Figure1.3:StructureofQuercetin

Quercetin is pentahydroxyflavone having five hydroxy groups.Three cyclic rings present in the structure among them two of them are phenyl groups. 2 hydroxy group present in each phenyl rings. The centre ringhave a double bond at its second and third position, fourth position contains carbonyl group and there also a hydroxy group present in thethird carbon.Thus it have a molecular formula of $C_{15}H_{10}O_7$ (Figure 1.3). The presence of Phenolic hydroxyl groups and double bonds endows quercetin with a strong antioxidant activity.

1.3.2 PARABROMOANILINE

p-Bromoaniline has a molecular formula C_6H_6BrN (Figure1.4). It is a chemicalinwhichtheparapositionofananiline molecule isreplacedwith a bromine atom. This substance is readily accessible for purchase and can be utilized as a building block, for example, in the Gomberg-Bachmann processto preparep-Bromobiphenyl. 4-Dihydroquinazolines and azo dyes are made using bromoaniline as a precursor. It is further added to the Moraxella sp. strain G growth medium as a carbon and nitrogen supplement [25].

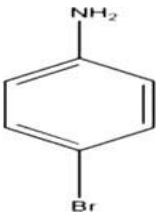


Figure1.4:Structureofp-Bromoaniline

1.3.3 2-AMINO-4-NITROPHENOL

2-amino-4-nitrophenol has a molecular formula $C_6H_6N_2O_3$ (Figure 1.5). 2,4-dinitrophenol reacts with sodium sulfide, 2-amino-4-nitrophenol is created (Farris, 1978).Agfa produced it for the first time in 1898 (Society ofDyers and Colourists, 1971).Atthe moment, hair coloring products use about 150 kg of 2-amino-4-nitrophenol.

The study examined the fungicidal properties of 2-amino-4-nitrophenol and its derivatives, which are produced by substituting various chemical radicals for the hydrogen atom in its amino group.When an aldehydegroup replaces the hydrogen atom in an amino group, the fungicidal activity against Rhizoctonia solani and Bipolaris sorokiniana increases. A ketone group substituted for the hydrogen atom amplifies the inhibitory impact on Venturia inaequalis and Sclerotinia sclerotiorum [26].

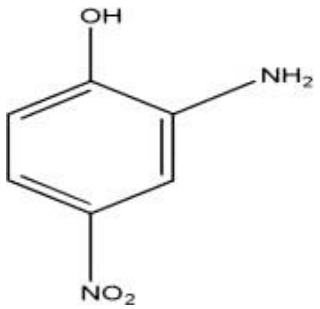


Figure1.5:structureof2-Amino-4-nitrophenol

1.3.4 2-AMINO-4-METHYLPHENOL

2-amino-4-methylphenol has a molecular formula C_7H_9NO (Figure1.6). Themainsensitizer incontactallergiesto DisperseYellow3 is2-amino-4-methylphenol.In100%ethanol, it combineswithacetylacetonetoproduce 4-(2-hydroxy-5-methylphenyl)imino2pentanone. It was changed byrefined human hemoglobin into dihydrophenoxazinone.

Tridentate with biological activity Schiff base ligands have been synthesized and studied using IR, elemental analysis, electronic spectrum data, molar conductance, and 1H NMR. These ligands are synthesized by reacting isatin with 2-amino-4-methyl phenol and their metal complexes, Ti (IV), Zr (IV), Cd (II), and Hg (II).Using disc diffusion techniques, the antibacterial activity of the Schiff base and its metal complexes has been investigated [13].

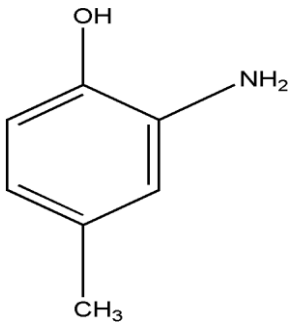


Figure1.6:Structureof2-Amino-4-methylphenol

1.3.5 ORTHOPHENYLENEDIAMINE

The formula for the chemical compound O-phenylenediamineis $C_2H_4(NH2)2$ (Figure 1.7).Anessentialprecursorto numerousheterocyclic compoundsisthisaromaticdiamine.OPDisawhitesubstance,however

airborne oxidation causes samples to seem darker. When combined with m- and p-phenylenediamine, it is isomeric.

Carbon nanodots (C dots)werecreatedusing a straightforward hydrothermal process using o-phenylenediamine (OPD). Carbon nanodots made from o-phenylenediamine are employed in cells to sense Cu 2+ ions.When stimulated at 420 nm, the C dots show photoluminescence at 567 nm. Cu(OPD)2 complexesoccur onthesurfacesofCdotswhenCu2+ ions are present, causing the color of the dots to change from yellow to orange and increasing the PL intensity[27].

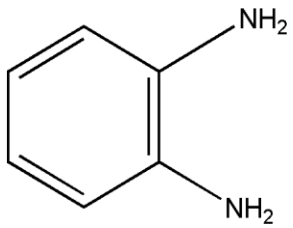


Figure1.7:Structureofo-Phenylenediamine

1.4 ANTI-INFLAMMATORYSTUDIESOFSYNTHESIZESCHIFF BASE

1.4.1 INFLAMMATION

Inflammationis the response of our body's immune system against the foreign body that enter into our body. Whenever our body encounters an outside invader likeabacteriaorvirus,toxinsorourbodysuffersaninjury our immune system gets activated and releases the substances into the blood called inflammatory markers. The job of these inflammatory markers is to trap the virus or bacteria or heal the injured tissue in case of an injury. These responses may in the form of redness or swelling of the wound.

There are two different types of Inflammation. ACUTE and CHRONIC inflammation.Acute inflammation are usually short term.Symptoms of acuteinflammationincludepain,redness,tendernessorswellingatthesite of the infection or injury.Actually acute inflammation is a protective response of the body that helps in healing the body from a infection or injury.

Whenthe bodykeepstriggering the immune systemto release white blood cells and other Inflammatory markers even there is no outside dangers. This inflammation is called chronic inflammation. Chronic inflammationis usually long lasting and it can go from a few months to few years. The symptoms of chronic inflammation is little vague and might include abdominal pain or discomfort join pain, fever etc, which may cause dangers to our body [28].

1.4.2 CAUSESOFINFLAMMATION

Acuteinflammationcanresultin:

• Painorsoreness;

• Blushedskinwherethedamageoccurred.

• Swelling.

• Temperature.

Inflammationthatischroniccanlastformonthsorevenyears.Itis associated with or may be associated with a number of disorders, including:

Diabetes,cardiovasculardisease(CVD),arthritisandotherjointdiseases, allergiesandchronicobstructivepulmonarydisease(COPD),rheumatoid arthritis, psoriasis [29].

1.4.3 PREVENTIONOFINFLAMMATION

The first and most effectiveAntiInflammatory measure that can follow is goodfood, nutrition, proper exercise etc.The topAntiInflammatoryfoods is turmeric .The compoundcurcumin in turmeric has been studied a lotfor combating inflammation in the body .Other compounds with effective AntiInflammatorypropertyare lutein ingreen leafyvegetables ,omega -3 fattyacids in fattyfishand walnuts , the greenmoong beanalsohasbeen found to have excellentAnti Inflammatory properties .Foods that should be completely avoided to prevent blood inflammationor reduce existing inflammation are processed foods , trans fat (Vanaspati Dalda) , avoid alcohol etc .There is no perfect test for detecting inflammation .Usually doctorsand medicalprofessionalsrecommend atest when inflammation is associatedwithothermedicalconditions.Doctorstreatinflammationby

putting patients onnonsteroidalAntiInflammatorydrugs like Ibuprofenor aspirin [30].

1.4.4 ANTI-INFLAMMATORYDRUGSANDITSEFFECTS

Non-steroidalanti-inflammatorydrugs (NSAIDs), whichact via inhibition of thecyclooxygenase (COX) isozymes, werediscovered more than 100 years ago. They continue to be an essential part of the pharmacological treatment of both acute and persistent pain.The biological activities of the COX-1andCOX-2isozymes are distinct; analgesic effectiveness is predominantly (butnotcompletely)linked toCOX-2inhibition, whereas theinhibitionhasdistinct adverseeffects.AllavailableNSAIDs, including acetaminophen and aspirin, are associated with potential side effects, particularly gastrointestinal and cardiovascular effects, related to their relative selectivity for COX-1 and COX -2 [31].

Ibuprofenwas first made available to people as an anti-inflammatory medication in England in 1967 and the US in 1974.Milligram for milligram, it possesses strong but mild anti-inflammatory qualities comparable to aspirin, but with much less detrimental effects on the stomach .Although ibuprofen, fenoprofen, and naproxen have a chemical relationship, this does not imply that none of the other members of this class of propionic-acid derivatives have any impact .The medication’s analgesic qualities are most likely a result of its anti-inflammatoryqualities .It is a nonsteroidal agent since it prevents the manufacture of prostaglandins and does not affect the adreno pituitaryaxis. Ibuprofen has been shown to be effective in rheumatoid arthritis and osteoarthritis and is probably effective in ankylosing spondylitis, gout, and Bartter's syndrome [32].

Chapter 2

LiteratureReview

AmandeepSodhiandhiscoworkersconductedastudyonsystemic autoimmune illness, rheumatoid arthritis (RA) and the effect of quercetin alone or mix with methotrexateoninflammation.Thetemporomandibular joint(TMJ)maybeimpactedbyRA,despitethefactthatthehands, wrists,andfeet arethejointsmost commonlyaffected.Disease-modifying antirheumaticDrugs(DMARDs)haveantiproliferative, immunosuppressive,andanti-inflammatoryactivity,controllingthe progressionofRA.Atthe moment, methotrexate(MX) istheinitial course oftreatmentforRA.ThecontinuousMXdosingmayinducepertinent adverseeffects,includingliverandrenaldamage,leukopenia,anddrug resistance. Evidencesuggests QT is atreatmentfor RA thatcanbe used because it increases synoviocyte apoptosis in cell culture, suppresses pro-inflammatory mediators, and modifies preclinical studieshave shownthat activatingtranscriptionfactorsignalingpathwaysimprovesclinical symptoms and lowers pro-inflammatory cytokines in RApatients'plasma levels.ThearthriticanimalstreatedwithQTand/orMXshoweda significantincreaseinthenociceptivethresholdwhencomparedto untreated arthritic animals. Results suggest that QT reduces inflammation andshowshepatoprotectiveeffectinanexperimentalmodelofRAinTMJ [33].

Fourcommonflavonolglycosidecompounds—luteolin, kaempferol,apigenin,andquercetin—arepresentinmanyplantswitha

variety of biological activity.Ruxia Wang,Yu Chang, Xin Liu,and some coworkersanalysed these4 flavonol glycoside compoundsandmeasured theNOlevel,phagocytosis,DPPHandABTSradicalscavenging activities,andferricreducingantioxidantpower.Thecurrentstudy concentrated on their antiinflammatory and antioxidant activities in vitro. Thisinvestigationshowedthatallfourdrugscouldlowerphagocytosis andNOconcentrations.Theirantioxidantactivitiesincreasedasthe concentrationincreased.TheIC50ABTSvalueswere0.59,0.8506, 0.8243,0.5083,1.4497and2.1563μg/mlforluteolin,kaempferol, apigenin,quercetin,BHTandVC,respectively.Theyconcludedthat quercetin is an ideal antioxidant and anti-inflammatorydrug that may be usedasanadjuvanttreatmentforoxidativestressandinflammatory illnesses,accordingtotestresults.Furthermore,thisstudyprovided preliminaryevidencethatthenumber ofphenolichydroxylgroupsdirectly correlateswithantioxidantactivity.Furthermore,compoundscontaining enolgroupsdemonstratedhigherantioxidantandanti-inflammatory activity compared to those lacking enol group [34].

MarijaLesjak,IvanaBearaandtheircolleaguesanalysedsix quercetinderivative.Sixquercetinderivatives(quercetin-3-O-glucuronide, tamarixetin,isorhamnetin,isorhamnetin-3-O-glucoside,quercetin-3,4′-di-Oglucoside,quercetin-3,5,7,3′,4′-pentamethylether)wereevaluatedfor theirantioxidantandanti-inflammatorypropertiesincomparisontothe activity of standard onionextract, which is the primarysource of dietary quercetin,andbenchmarks(butylatedhydroxytolueneandaspirin).The quercetincompoundsexhibitednoteworthybioactivitiesthatwere comparable to those of onions andstandards. The antioxidant efficacy of quercetinwasreduceduponderivatizationofitshydroxylgroups. Nevertheless,therewasnoclearrelationshipbetweenquercetin'sabilityto

prevent the synthesis of inflammatory mediators and the quantity of free hydroxylgroupsinit.Insummary,thesystemiccirculationofquercetin derivativesfollowingquercetinconsumptionmayfunctionasstrong antioxidants and anti-inflammatory agents, as well as enhance the overall biological activity ofa diet rich in quercetin [35].

Using amousemodel of asthma, A. P. Rogerio, L. H. Faccioli and theircolleaguesexaminedtheanti-inflammatorypropertiesofquercetin andisoquercitrin.Afterreceivingtwointranasalovalbuminchallenges, BALB/cmicereceivedanimmunization(ovalbumin/aluminumhydroxide, s. c.).Aftertheinitial immunization,themiceweregivendailygavages of either quercetin (10 mg/kg) or isoquercitrin (15 mg/kg).Positive control: 1mg/kg,s.c.of dexamethasonewasgiven. Twenty-fourhoursfollowing thefinalovalbuminchallenge,leucocyteswereexaminedinlung parenchyma,blood,andbronchoalveolar lavagefluid(BALF).We examinedinterleukin-5(IL-5)inlunghomogenatesandBALF.Effective eosinophilicinflammatorysuppressors,quercetinandisoquercitrinmay have therapeutic value in the treatment of allergies [36].

Potentialapplicationoftheantioxidantquercetintoshieldcellsfrom intracellularCa2+overload:amodelexperimentconductedbyYumiko Nishimuraandhis coworkers. It is well knownthat quercetin shields cells from oxidative damage. One of the processes that causes cell death is the elevationofintracellularCa2+contentbroughtonbyoxidativestress. Thus,theypostulatedthatquercetinmightshieldcellsthatare experiencinganexcessofintracellular calciumions. Usingrat thymocytes andaflowcytometerfittedwithappropriateflourescenceprobes,the effectsofquercetinoncellsexperiencingintracellularCa2+excessand oxidativestresswereinvestigatedinordertotestthetheory.The concentrationsofquercetin(1–30μM)usedtoprotectcellsfrom

intracellularCa2+overloadcausedbyacalciumionophorewere comparabletothoseusedtoprotectcellsfromH2O2-inducedoxidative stress.When external Ca2+ was removed, the celldeath caused by H2O2 andcalciumionophore,respectively,wasgreatlyreduced.Moreover, quercetindramaticallypostponedtheCa2+-dependentcelldeathprocess whilehavingnodiscernibleeffectontheincreaseinintracellularCa2+ concentrationcausedbycalciumionophoreandH2O2,respectively. Conclusionisthat,Despiteanincreaseinintracellular Ca2+concentration, quercetin can shield cells from oxidative damage.The findings imply that quercetin is alsoemployed toshieldcellsfrom intracellular Ca2+excess [37].

ShankarANandhiscoworkersexaminedtheinvitroantibacterial activityofquercetinandits1-6derivativesagainstBacilluscereus, Salmonellaspp., Escherichiacoli, andStaphylococcus aureus in addition toitsinvitroantioxidantactivityagainstDPPH freeradical.Withthe exceptionofcompounds3and4,whichhadincreasedantibacterial activity against Escherichiacoliwhencompared toquercetin, the results showedthatalltheinvestigatedderivativesof quercetinhadless antioxidantandantibacterialactivitythanquercetinitself. Theycameto theconclusionthatquercetinhadbetterantioxidantandantibacterial activity than its 16 derivatives at the testedconcentrations. However, the invitroantibacterialactivityresultsforcompounds3and4showa significantimprovementinthegram-negativeantibacterialactivityagainst Escherichia coli when compared to quercetin [38].

AliDehghaniandhisassociatespublishedastudyintheJournalof MolecularLiquidsin2020,volume309,page113035.Theprotective behaviorofquercetin,aflavonoidgroupofpolyphenols,wasthoroughly

investigatedinthestudyusingtestsandprecisemodeling(including molecular/atomic-levelsimulations,MD/MCaugmentedwithDFT)inHCl acidicenvironment(containing1M).TheQuercetincompound's structuralcharacterisationwasachievedbytheapplicationofbothUV-Vis andFT-IRtechniques.FE-SEM,AFM,andcontactangleanalyseswere usedtoinvestigatethesurfaceprotectivefeatures.Resultsshowedthat steelis protectedfromcorrosionattacks bythecoatingandshielding providedbyquercetinmolecules.Afteronehourof metalsubmission, protectiondegreesofroughly95%and93%,respectively,wereattained basedontheEISandweightlossmeasures.Throughacombined cathodic/anodicmechanism,quercetinmoleculescanrestrictcorrosion activities,asdemonstratedbythepotentiodynamicpolarizationcurves. Furthermore,itwasobservedthattheformationofamono-protective layer wasguaranteedbytheadsorptionofquercetinmoleculesin accordancewiththeLangmuirisotherm.TheDFTsimulationssuggestthat adonor-acceptorinterfacialmechanismmaybeinvolvedinthe interactionsbetweentheQuercetin/ironcomplexationsandthetarget metallicadsorbent.Furthermore,theMC/MDtechniquesguaranteedthe adsorption of metal-organic complexes on the iron surface [39].

TheworkdonebyMoamenSRefatandhiscoworkers aimedtoassesstheanti-inflammatoryandantioxidantpropertiesofthe novel[Ru(Q)(Cl)2(H2O)2] complex(Ru(III)/Q).Anovelimportant combination comprising ruthenium (III)ions and theflavonoidmolecule quercetin (Q) wascreated. Investigation of the Ru (III)/Qcomplex using infrared (FTIR) spectroscopyrevealed thatQ iscoordinatedas a bidentate withRumetalions.TheRu(III)complex'soctahedralgeometrywas identified by the magnetic susceptibility value (1.85 B.M.)and electronic (UV−Vis)spectra.Accordingtothethermogravimetricresearch

(TG/DTG),theRu (III)/Qcompoundisfairly stableupto300 °C.60 male ratsweredivided intosixgroups inordertomeasurebiological activity. The comet assay was carried out in the brain tissue, while cytokines were measuredinthetesticularandbraintissuesusinghistologicaland ultrastructuralinvestigations.AdministrationofRu(III)/Q,either byalone orinconjunctionwithDG,inhibitedapoptoticactivitiesandbrought oxidativedamagedowntonormallevels.Ru(III)/Qthusdecreased oxidative stressin male ratsand prevented damage to the brain and testes. D-galactose(DG)inducedagingneurotoxicity,reproductivetoxicity,and antihepaticcanceractionareallsignificantlymitigatedbythe(Ru (III)/Q) complex [40].

It is commonly recognized that the genus Bifidobacterium has positivehealth effects.Yoshikiyo okada,Yoshikazu Tsuzuki and their coworkersfoundthatBifidobacteriumadolescentissecretedmoreanti-inflammatorycompoundswhenexposedtoquercetinandrelated polyphenols.Theirstudylookedintothepropertiesoftheanti-inflammatorycompoundsthatB.adolescentissecretes.Quercetin-infused B.adolescentisculturesupernatantloweredactivatedmacrophagelevels ofinflammatorymediators.Whiletheelevationofantiinflammatory activitybyquercetinpersistedafterquercetinwashout,spontaneous quercetindegradantwasunabletopromoteanti-inflammatoryactivity.The culturesupernatant'sbioactivecomponentsmaybeheat-stable,non-phenolic,acidicbiomolecules withmolecular weightslessthan3kDa, according to physicochemical analysis. There is no impact of acetate and lactateonthegenerationofnitricoxide.Whencombined,B.adolescentis's anti-inflammatorycompoundsmightbetinymoleculesratherthanshort chainfattyacids.Theseresultsledtotheprovisionalidentificationof stearicacidasabioactivecandidatechemical[41].

Chapter 3

MaterialsandMethods

3.1 REAGENTS

Allthereagentswereusedasanalyticalgrade,purchasedfromSigma Aldrich and were used as received.

i. Quercetin
ii. Parabromoaniline
iii. 2-amino-4-nitrophenol
iv. Orthophenylenediamine
v. 2-Amino-4-methylphenol

3.2 SOLVENTS

Solvent used for the synthesis and purification procedure were purchased from spectrochem Ltd and used without further purification.

i. Methanol
ii. Ethanol
iii. PetroleumEther
iv. DMSO

3.3 PHYSICAL-CHEMICALMETHODS

3.3.1 ELEMENTALANALYSIS

CHNElemental Analysisprovidesameasureofcarbon,hydrogen,and nitrogenelementalcontentinasample.Itcanbeusedonawiderangeof

sample types including solids, liquids, and volatile substances. It helps to determine the structure of the sample substance by knowing the composition of the elements. it gives a pure and accurate measurement of the elements present in a sample. CHN elemental analysis is based on the combustionofthesample.Uponcombustion,thesamplegeneratesuniform compound gases of elements C, H, and N. Then it is measured using gas chromatography [42].

CHN ElementalAnalysis was recorded at the SAIF, Cochin University of Science and Technology, Kochi, India.

3.3.2 INFRAREDSPECTROSCOPY

IR is the electromagnetic radiation with a longer wavelength than visible light. IR Spectroscopy studies the interaction between matter and IR radiation. Two compounds will never show similar IR spectra. Compound or sample have change in dipole moment during vibration is the major requirementofIRSpectroscopy.Sinceeachtypeoflinkhasauniquenatural frequencyofvibration,notwomoleculeswithdifferentstructureswillhave exactlythesame infraredabsorptionpattern,orinfraredspectrum, because two molecules of the same type in two distinct compounds are in two slightly different environments [43].

An infrared spectrometer, or more accurately a spectrophotometer, is the device that measures a compound's absorption spectrum. The organic laboratory often uses two types of infrared spectrometers: dispersive and Fourier transform (FT) devices. These two kinds of equipment offer compoundspectrainthesharedrangeof4000Upto400cm−1.Foragiven molecule, the two generate virtually similar spectra; however FT provides the spectrum more rapidly than dispersive instruments.

Infrared spectra were recorded in the range 4000-400 cm^{-1}at Department of Chemistry, Bharata Mata College, Thrikkakara, Kochi, India.

3.3.3 ULTRAVIOLETSPECTROSCOPY

In the sections of the electromagnetic spectrum known as the ultraviolet (UV) and visible (VIS) regions, or the range of wavelengths from190 nm to 800 nm, the majority of organic molecules and functional groups are transparent. As a result, absorption spectroscopy is not very useful in this wavelength range. Nevertheless, these parts of the spectrum can occasionally yield useful information. When paired with the specifics offered by nuclear magnetic resonance (NMR) and infrared spectra, that data can reveal important structural proposals. The main principle is the Beer Lamberts Law. Molecules containing bothbonding and non-bonding electrons absorb energy and get excited to higher energy levels. There can be four possible types oftransitions (π-π*, n-π*, σ-σ*, and n- σ*), and the following is their order of energy: σ- σ* > n- σ* > π-π* > n-π* [44] .

Ultraviolet-VisibleSpectroscopywererecordedintherange200to 700 nm at Department of zoology, St. Teresa's College (Autonomous), Ernakulam, Kochi, India.

3.3.4 NUCLEARMAGNETICRESONANCESPECTROSCOPY

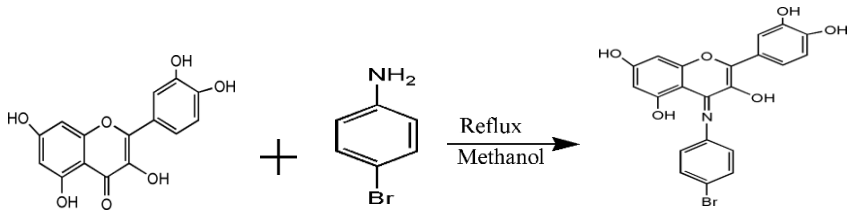
Nuclear Magnetic Resonance spectroscopy is a technique used to study molecules. It involves recording the interactions between radio frequency electromagneticradiationandthenucleiofmolecules inastrong magnetic field. NMR Spectroscopy is used in research and quality control. It can determine the purity and content of a samples well as its molecular structures.Italsoanalysesmixturesthatcontainsknowncompounds.NMR

Spectroscopy is based on the reorientation of atomic nuclei with non-zero nuclear spin in an external magnetic field.NMR Spectroscopy provides bothquantitative and qualitative dataonthe compositionofa sample [45]. NMR spectroscopy was recorded in the range 0-20 ppm for H^1NMR and 0-220 ppm for $C1^3$NMR at Department of Applied Chemistry, Cochin University of Science and Technology, Kalamassery, Kochi, India.

3.4 SYNTHESISOFSCHIFFBASE

3.4.1 Synthesis of Schiff Base from Quercetin and p-Bromoaniline

Quercetininmethanolandp-Bromoanilineinmethanolwerecombinedin a1:1ratio and heated for 6hoursunder refluxinanRB flask. (Scheme1). Aftercoolingandbeingconcentrated,theresultantsolutionwasgiventime for slowevaporation.After filtering, collecting, andwashingwithethanol, the precipitate that had a light green hue was recrystallized and dried. The crystals were collected (Figure 3.1).



Scheme1:PreparationofQPBA

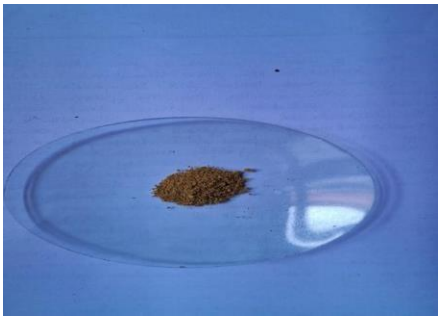
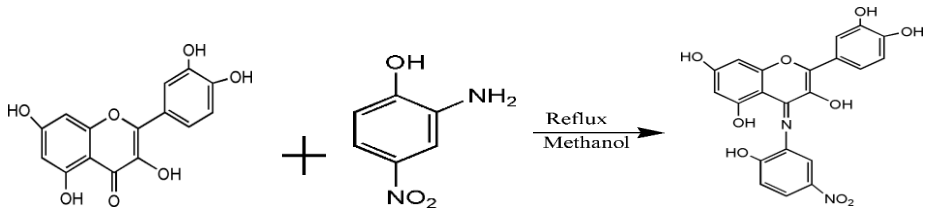


Figure3.1:Crystalsof QPBA

3.3.2 Synthesis of Schiff Base from Quercetin and 2-amino-4-nitrophenol

Quercetin in methanol and 2-Amino-4 -nitrophenolin methanol were combined ina1:1ratio and heatedfor 6hoursunder refluxinanRB flask. (Scheme2).Aftercoolingand beingconcentrated,theresultant solutionwas given time for slow evaporation. After filtering, collecting, and washing with ethanol, the precipitate that had a greenish yellow hue was recrystallized and dried. The crystals were collected (Figure 3.2).



Scheme2:PreparationofQANP

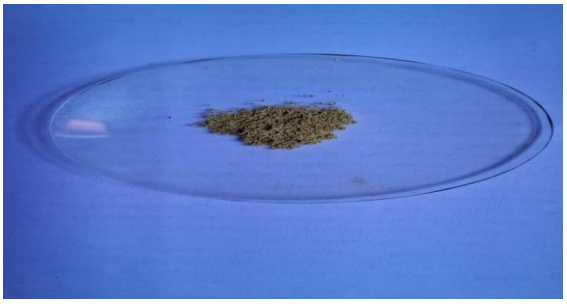
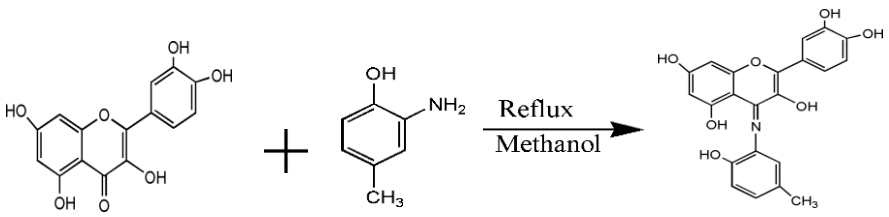


Figure3.2:CrystalsofQANP

3.3.3 Synthesis of Schiff Base from Quercetin and 2-Amino-4- methylphenol

Quercetin in methanol and 2-Amino-4-methylphenol in methanol were combined ina 1:1ratio and heated for6hoursunder reflux inanRB flask (Scheme 3). After cooling and being concentrated, the resultant solution was given time for slow evaporation. After filtering, collecting, and washing with ethanol, the precipitate that had a brownish yellow hue was recrystallized and dried. The crystals were collected (Figure 3.3).



Scheme3:PreparationofQAMP

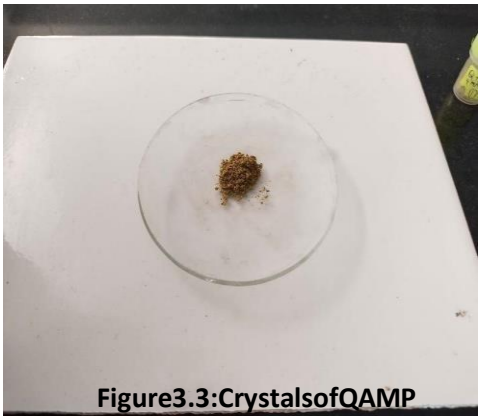
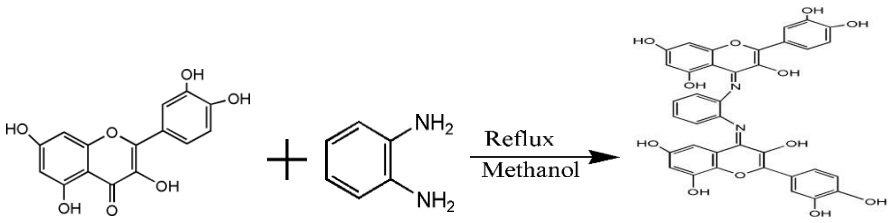


Figure3.3:CrystalsofQAMP

Figure3.3:CrystalsofQAMP

3.3.4 SynthesisofSchiffBasefromQuercetinando-Phenylenediamine

Quercetin in methanol and o-Phenylenediamine in methanol were combined in a 1:1 ratio and heated for 6 hours under reflux in anRB flask (Scheme4).Aftercoolingand beingconcentrated,theresultant solutionwas given time for slow evaporation. After filtering, collecting, and washing with ethanol, the precipitate that had a light brown hue was recrystallized and dried. The crystals were collected (Figure 3.4).



Scheme4:PreparationofQOPD

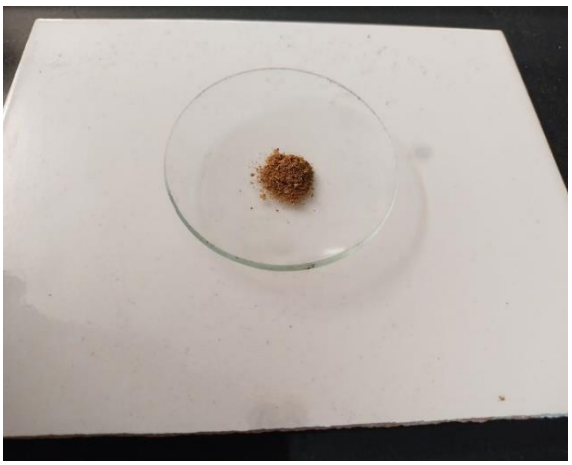


Figure3.4:CrystalsofQOPD

3.4 ANTIINFLAMMATORYSTUDYOFSCHIFFBASE

3.4.1 MATERIALSUSED

i. HumanBlood

ii. AlseverSolution

iii. Isosaline

iv. Schiffbases

3.4.2 PROCEDUREFORANTI-INFLAMMATORYACTIVITY

Plant extracts'ability to reduce inflammation was evaluated using the in vitro HRBC membrane stabilization technique. Fresh whole human blood (10ml) was collected and transferred to the heparin zed centrifuged tubes. The collected blood was mixed with an equal volume ofAlsever solution (dextrose 2%, sodium citrate ,0.8%, citric acid 0.05%, sodium chloride 0.42%,anddistilledwater100mL)andcentrifugedwithisosaline(0.85%, dissolve 8.5g NaCl in water). Autoclave 15 min at 121°C. Cool to room temperature.To 1mL of HRBC suspension, an equal volume of plant extracts in three different concentrations (10 mg/ml, 5 mg/ml and 2.5 mg/ml) was added. All the assay mixtures were incubated at 37°C for 30 Minutes and centrifuged. Using a spectrophotometer set at 560 nm the amount of hemoglobin in the supernatant solution was calculated. The percentage of protection can be hence calculated from the equation as given,

Percentofprotection =100-ODoftest/ODofcontrol×100

Chapter 4

Results anddiscussion

4.1 ELEMENTALANALYSIS

The Elemental Analysis obtained matches with the assigned chemical formula of the proposed structure of Schiff Bases. The calculated C, H,N persentageoftheSchiffBasesQPBA,QANP,QOPDandQAMParegiven in (Table 4.1):

Compound	**Empirical Formula**	**Formula weight**	**Colour**	**Observedand Calculated (%)**		
				C	**H**	**N**
QPBA	$C_{21}H_{14}BrNO_6$	456.24	Light Green	55.28 (55.31)	3.09 (3.12)	3.07 (3.1)
QANP	$C_{21}H_{14}N_2O_9$	438.34	Greenish Yellow	57.54 (57.57)	3.22 (3.25)	6.39 (6.42)
QOPD	$C_{36}H_{24}N_2O_{12}$	676.58	Light Brown	63.91 (63.94)	3.58 (3.61)	4.14 (4.17)
QAMP	$C_{22}H_{17}NO_7$	407.37	Brownish Yellow	64.86 (64.89)	4.21 (4.24)	3.44 (3.47)

Table4.1:ElementalAnalysis

4.2 INFRAREDSPECTROSCOPY

ThepeaksshowntheIRAbsorptionspectrumgiveimportantinformation aboutthedifferent functionalgroupspresent inthe SchiffBase(Figure4.1 – 4.4). The peak obtained in the range 1690-1640 cm^{-1}[46], indicates the presence of the imine (C=N) group. The peaks obtained in the 3600-3200 cm^{-1}[47], range indicate the phenolic (OH) group.FT-IR spectralbands of Schiff bases and their spectra are given in(Table 4.2).

Compound	**υ(OH)**	**υ(C=N)**
QPBA	3286.45	1662.95
QANP	3588.05	1661.96
QOPD	3385.77	1662.95
QAMP	3372.18	1661.35

Table4.2:InfraredspectraldataofSchiffBases

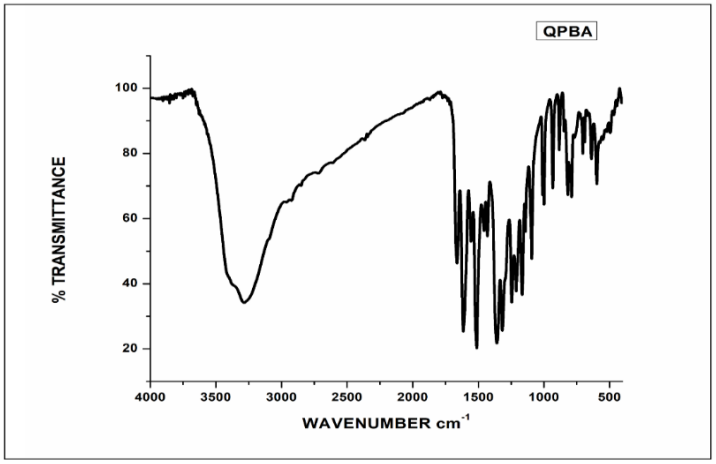


Figure4.1:IRspectrumofQPBA

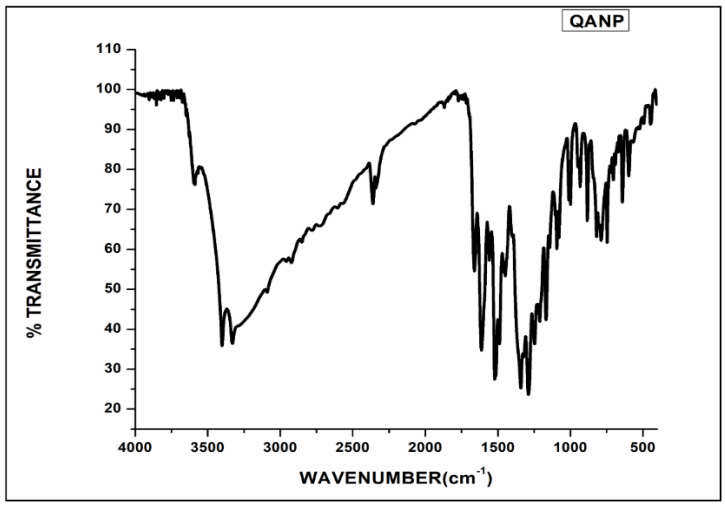


Figure4.2:IRspectrumofQANP

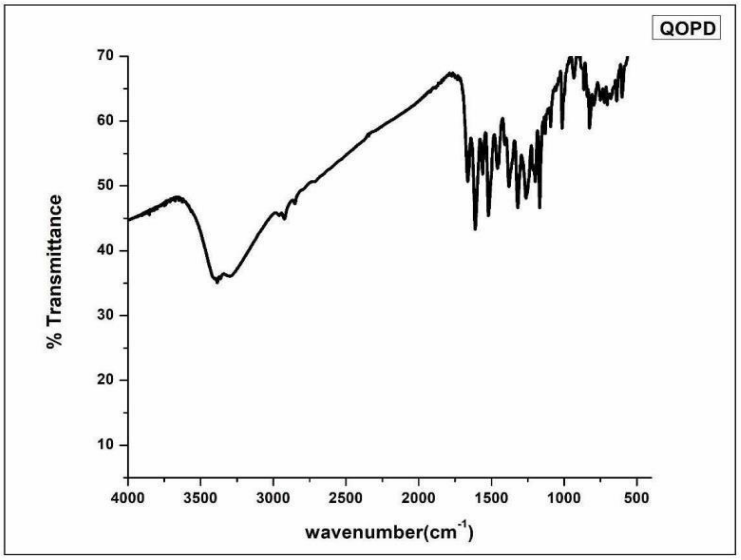


Figure4.3:IRspectrumofQOPD

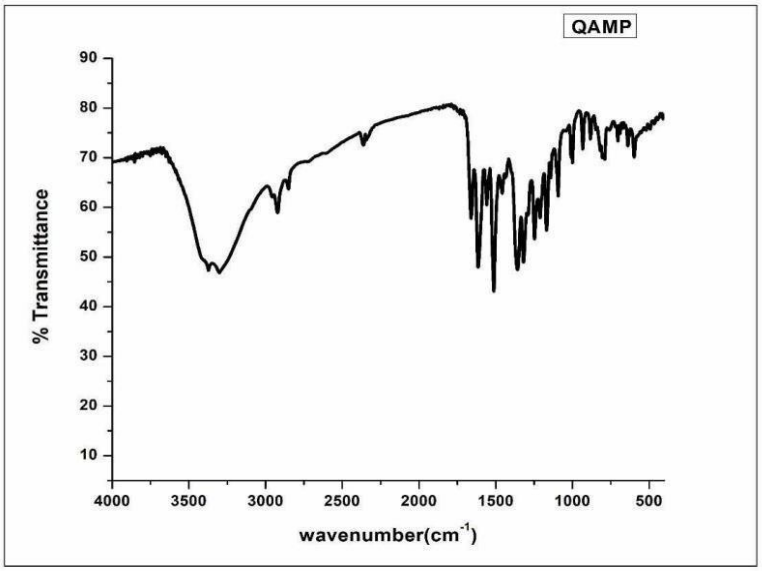


Figure4.4:IRspectrumofQAMP

4.3 UV-VISIBLESPECTROSCOPY

UV-Visible Spectroscopy is used to study the electronic structure and its dynamics in atom and molecules. The UV-Visible spectra of compounds QPBA,QANP,QOPDandQAMPweretakeninMethanolFigure(4.5-4.8) The range 200-260 nm is due to π – π* transitions [48]. And 350-400 nm represent n –π* transitions [49]. The spectral data are given in the (Table 4.3):

Compound	**n–π***	**π– π***
QPBA	369	254
QANP	372	256
QOPD	372	256
QAMP	369	256

Table4.3:UVvisiblespectraldataofSchiffBases

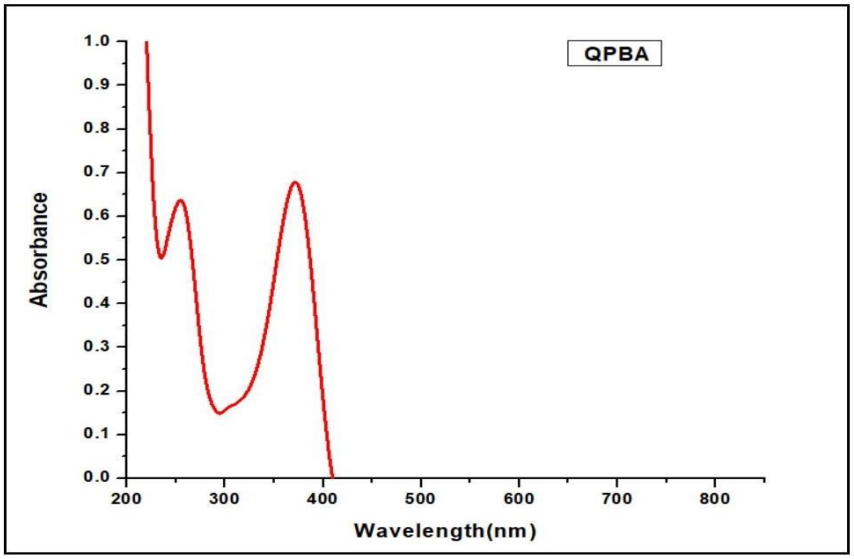


Figure4.5:ElectronicspectrumofQPBA

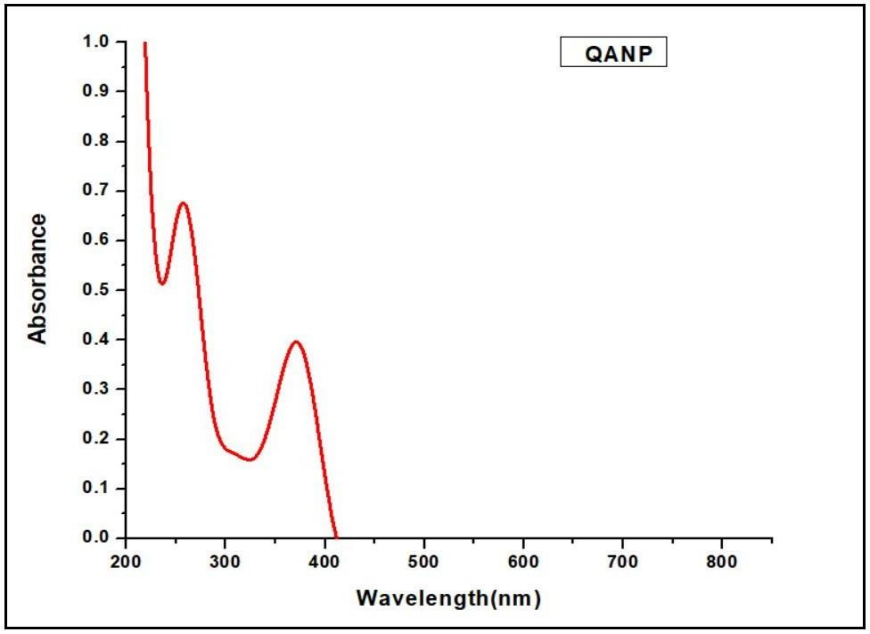


Figure4.6:ElectronicspectrumofQANP

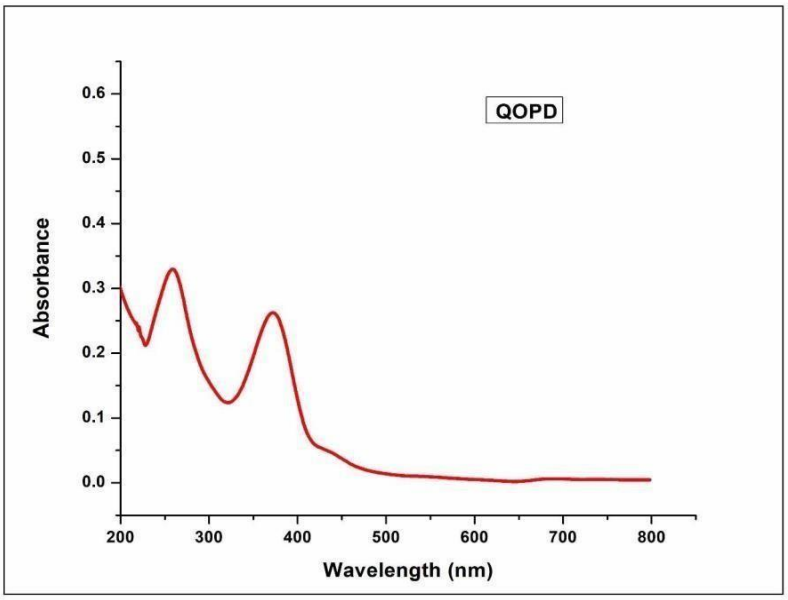


Figure4.7:ElectronicspectrumofQOPD

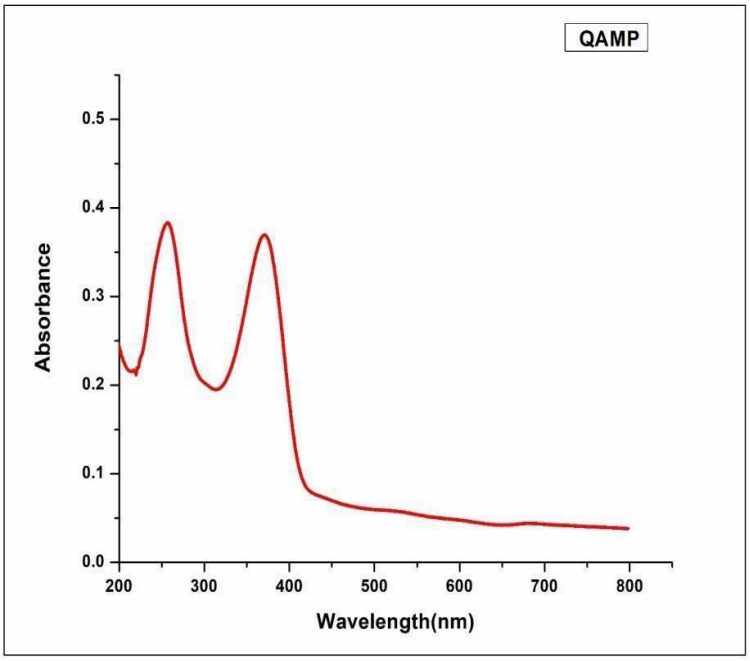


Figure4.8:ElectronicspectrumofQAMP

4.4 NUCLEARMAGNETICRESONANCESPECTROSCOPY

NMRcanbeusedto determine molecularconformationinsolutionaswell as study physical properties at the molecular level such as conformational exchange,phasechanges,solubility,anddiffusion.TheSchiffbase'sH[1]and C[13]NMRspectrumisrecordedinDMSOusingTMSasaninternalstandard shownin(Figures4.9–4.16).Thechemicalshiftvaluesofdifferentprotons obtained are as in (Table 4.4):

COMPOUND	**ASSIGNMENTS**
QPBA	**^{1}H NMR(DMSOδppm);**6.2(Ar-H),6-4(1H,Ar-H), 6-8(IH,Ar-H),7.5(1H,Ar-H),7.8(1H,Ar-H),9.4 (2H,OH),9.7(1H,0H),10.9(1H,OH),12.5(1H,0H). **^{13}CNMR(DMSOδppm);** 93.84(Ar-C), 98.62(Ar-C),103.46(Ar-C,115.49,116.05(Ar-C),120.42 (Ar-C),122.39(A2C),136.19(ArOH),145.50(Ar-OH), 147.23(Ar-C-OH),148.15(Ar-C0),156.57(Ar-CO),161.17(Ar-C-OH),164.33(Ar-C-OH),176.29 (ArC=N).

QANP	**^{1}H NMR(DMSOδppm);** 5.2 (1H,Ar-H), 6.2 (1H,Ar-H),6.4(1H,Ar-H),6.8(IH,Ar-H),6.9(1H,Ar--H),7.45(1H,Ar-H),7.7(1H,Ar-H),9.4(2H,Ar-OH), 9.6(1H,Ar-OH),10.8(1H,Ar-0H),12.5(IH,Ar-OH). **^{13}CNMR(DMSOδppm);** 93.80(Ar-C), 98.62(Ar-C), 103.45(Ar-C), 108.09(Ar-C),113.53(Ar-C),113-56(Ar-C),115.49(Ar-C),116.05(Ar-C), 120.42 (Ar-C),122.39 (Ar-C), 136:19 (Ar-C-OH),138.07 (Ar-C-OH), 140.61 (Ar-C-0H), 145.50(Ar-C-0H),147.03(Ar-C-OH),148.14(Ar-C-OH),151.16(Ar-C-OH),156.57(Ar-C0),176.29 (C=N).
QOPD	**^{1}HNMR(DMSOδppm);**6.1(2H,Ar-H)6.3(3H,Ar-H),6.5 (2H,Ar-H),6.8(3H,Ar-H),6.9(2H,Ar-H) ,7.5(2H,Ar-H),7.7(2H,Ar-H),9.4(5H,Ar-OH),12.5 (2H,Ar-OH). **^{13}CNMR(DMSOδppm);** 93.80(Ar-C), 98.66(Ar-C),103.46(Ar-C),115.04(Ar-C),115.52(Ar-C), 116.05 (Ar-C),117.79(Ar-C),120.44(Ar-C),122.42 (Ar-C), 135:36 (Ar-C),136.19(Ar-C-OH),145.51(Ar-C-0H), 147.24 (Ar-C-OH), 148.15(Ar-C-OH),156.60(Ar-C-OH),161.18(ArC=O),164.37(Ar-CO),176.29 (C=N).

QAMP	**^{1}HNMR(DMSOδppm);**2.07(3H,ArH),4.45(1H,Ar-H), 6.2 (1H,Ar-H), 6.4 (2H,Ar-H) ,6.6(1H,Ar-H), 6.9(1H,Ar-H),7.6(1H,ArH),7.7(1H,Ar H)8.67(1H,Ar-H),9.37(3H,Ar-OH),12.5(1H,Ar-OH). **^{13}CNMR(DMSOδppm);** 93.81(Ar-C), 98.64(Ar-C),103.45(Ar-C),114.69(Ar-C),115.51(Ar C),115.68(Ar-C),116.05(ArC),117.19(Ar-C), 120.43(Ar-C),122.41(Ar-C),136:19(Ar-C-OH),136.69 (Ar-C-OH),142.21(Ar-C-0H), 145.51(Ar-C-0H),147.24(Ar-C-OH),148.15(Ar-C-OH),156.59(Ar-C-O),161.17(Ar-C0),176.29 (C=N).

Table4.4:H^{1}andC^{13}NMRspectraldataoftheSchiffBases

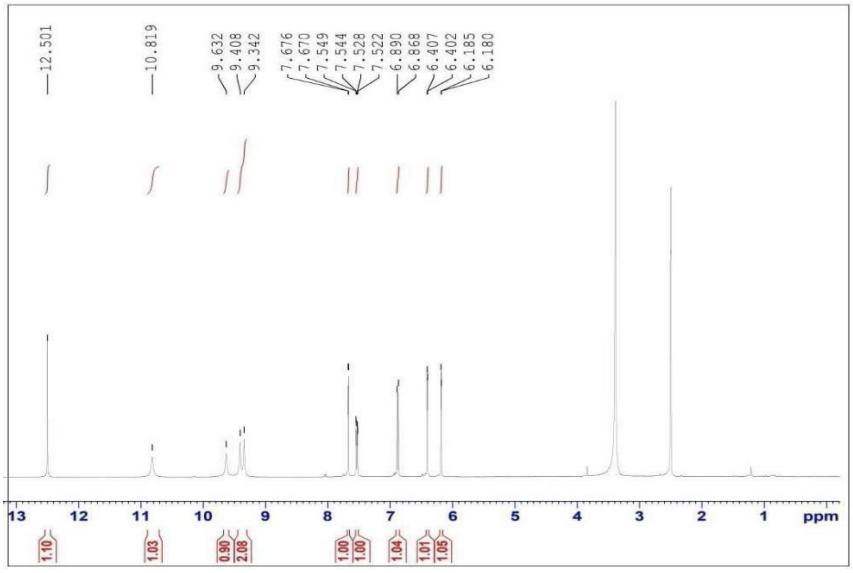


Figure4.9:^{1}HNMRspectrumofQPBA

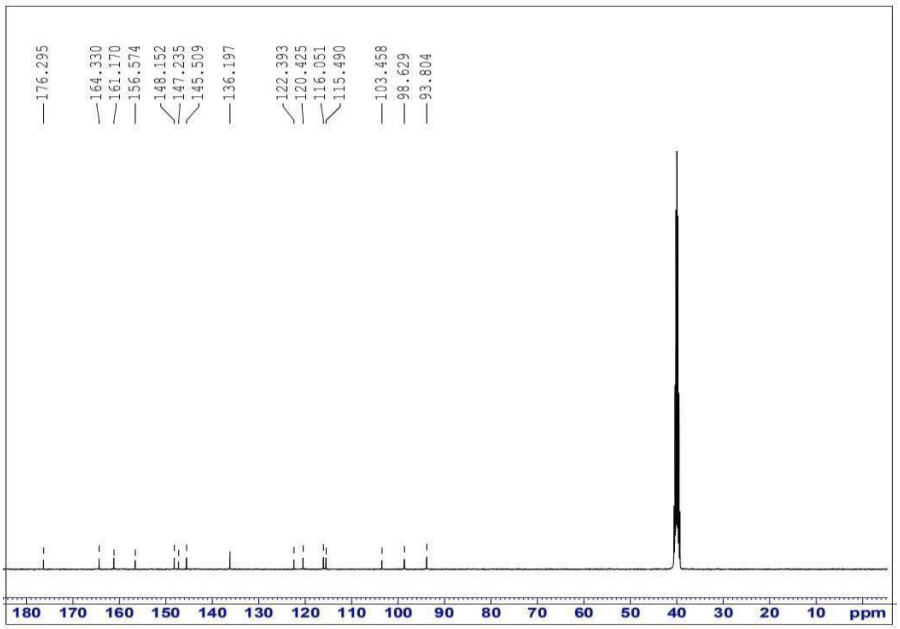


Figure4.10:C[13]NMRspectrumofQPBA

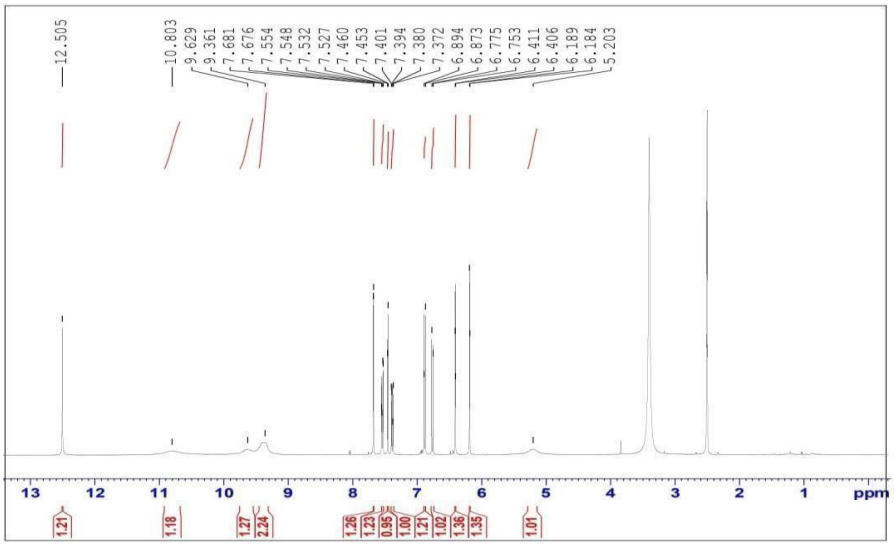


Figure4.11:H[1]NMRspectrumofQANP

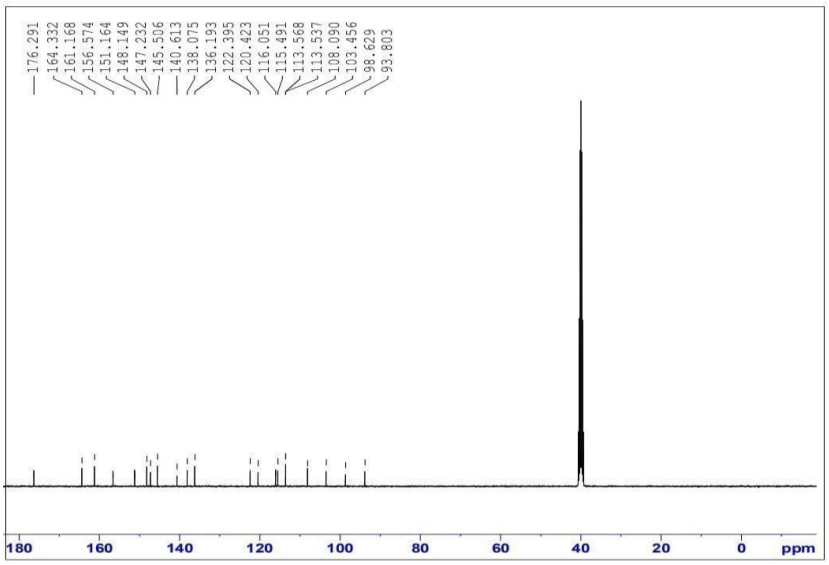


Figure4.12:C^{13}NMRspectrumofQANP

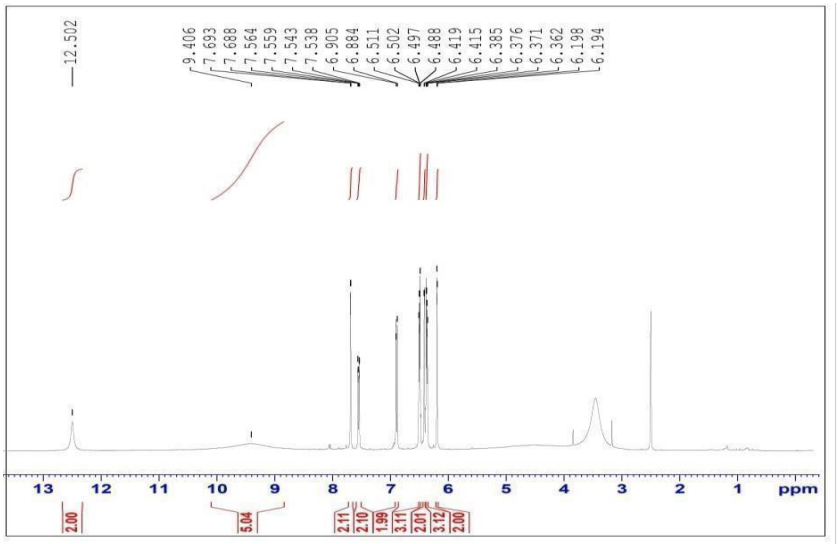


Figure4.13:H^{1}NMRspectrumofQOPD

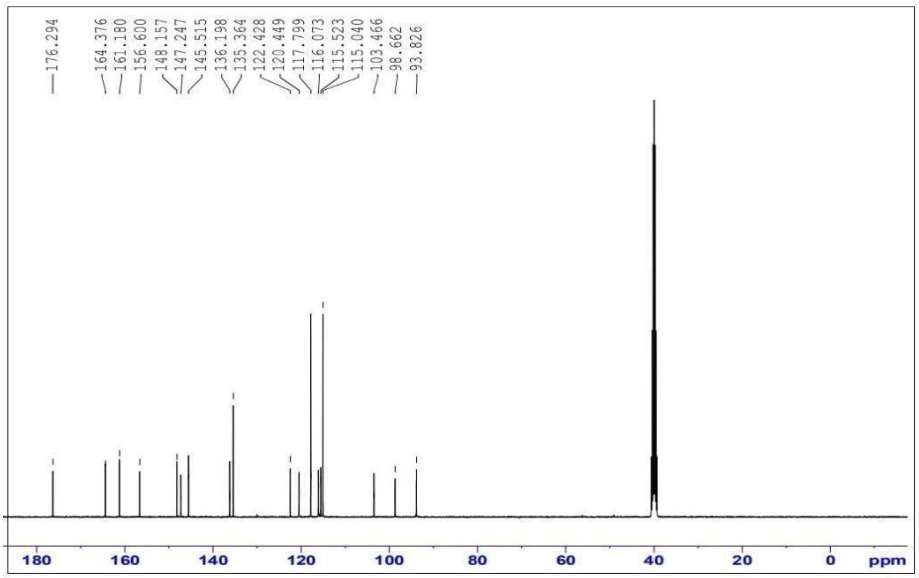


Figure4.14:C[13]NMRspectrumofQOPD

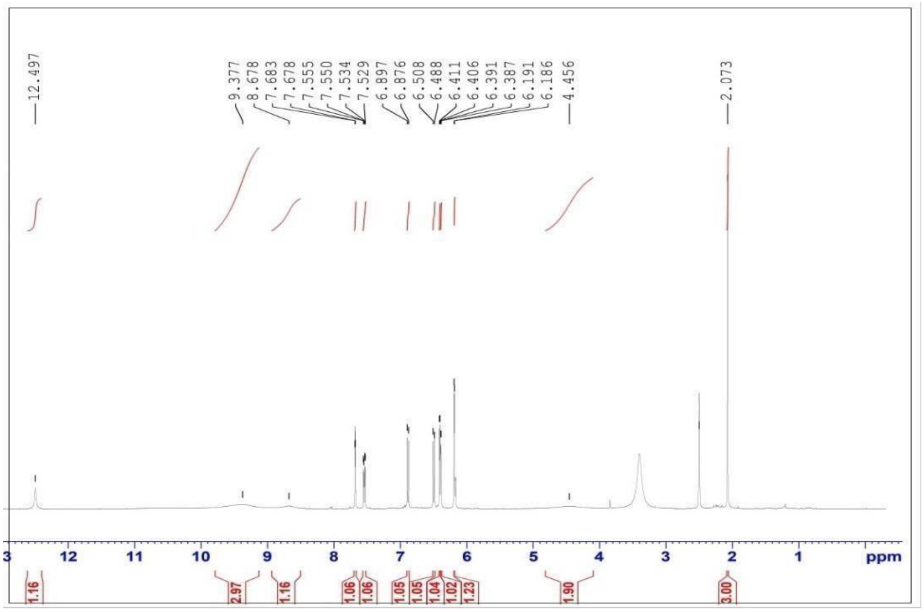


Figure4.15:H[1]NMRspectrumofQAMP

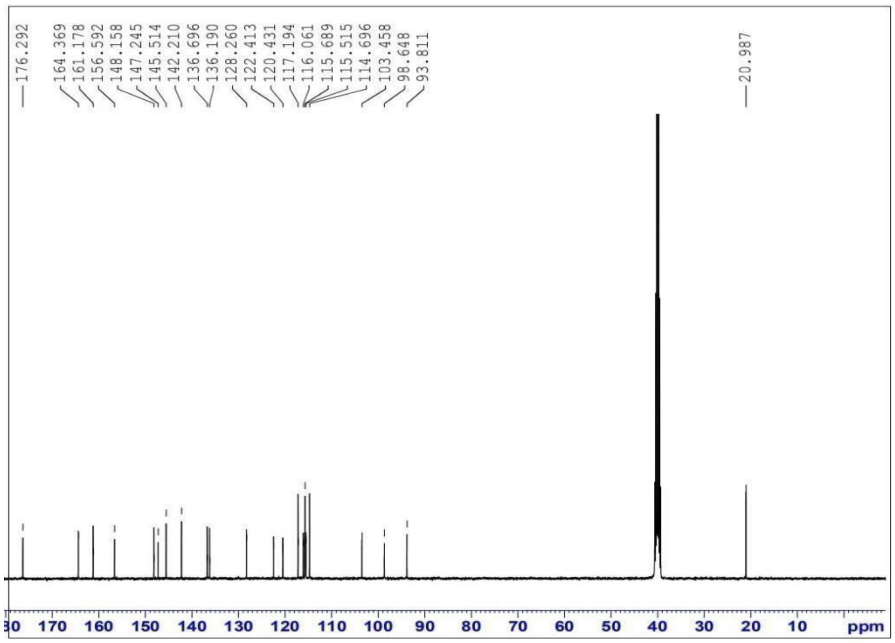


Figure4.16:C^{13}NMRspectrumofQAMP

4.1.5ANTIINFLAMMATORYACTIVITY

The anti-inflammatory activity of the Quercetin Schiff Bases was studied usingtheHRBCmembranestabilizationmethod.The%ofinhibitionofthe fourcompoundsatdifferentconcentrationswascalculated.Thepercentage of inhibition values of QPBA, QANP, QOPD, QAMP were tabulatedin Tables4.5-4.8.TofindtheIC50valueoftheQuercetinSchiffbasesagraph was plotted with values % of inhibition against the concentration of the sample which is shown in (Figures 4.16-4.18).

QPBA

Concentration of sample(mg/ml)	**% of Inhibition**
2.5	34.5
5	57
10	74.9

Table4.5:Anti-inflammatoryactivityofQPBA

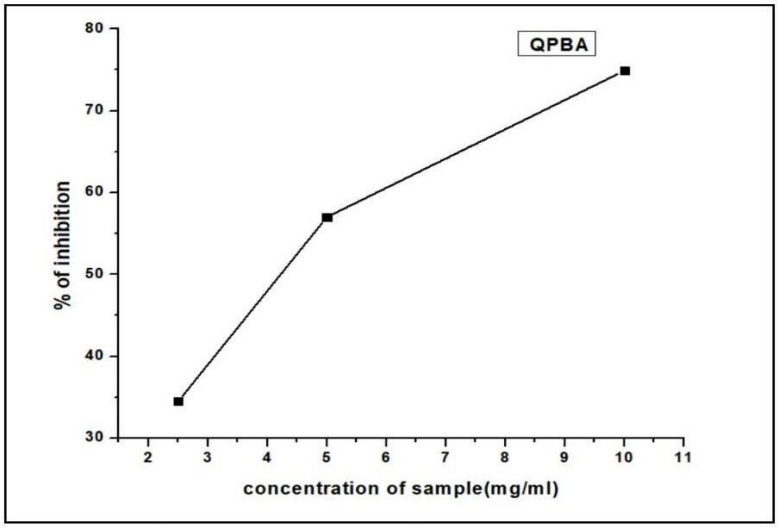


Figure4.16:Anti-inflammatoryofQPBA

QANP

Concentration of sample(mg/ml)	**%ofInhibition**
2.5	34.7
5	40.4
10	54.9

Table4.6:Anti-inflammatoryactivityofQANP

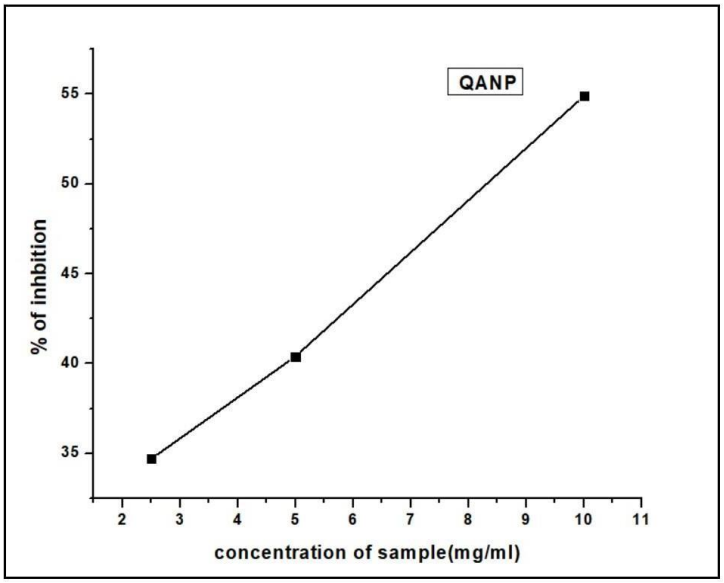


Figure4.17:Anti-inflammatoryofQANP QOPD

Concentration of sample(mg/ml)	**%ofInhibition**
2.5	34.6
5	42.3
10	53.1

Table4.7:Anti-inflammatoryactivityofQOPD

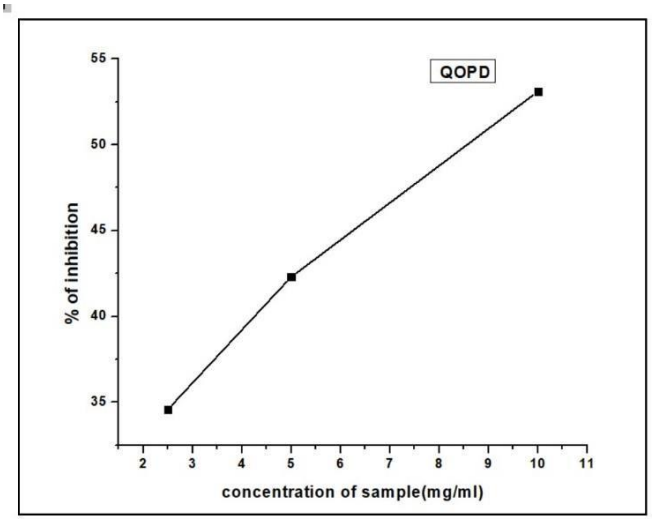


Figure4.17:Anti-inflammatoryofQOPD

QAMP

Concentration of sample(mg/ml)	**%ofInhibition**
2.5	32.4
5	41
10	51.2

Table4.8:Anti-inflammatoryactivityofQAMP

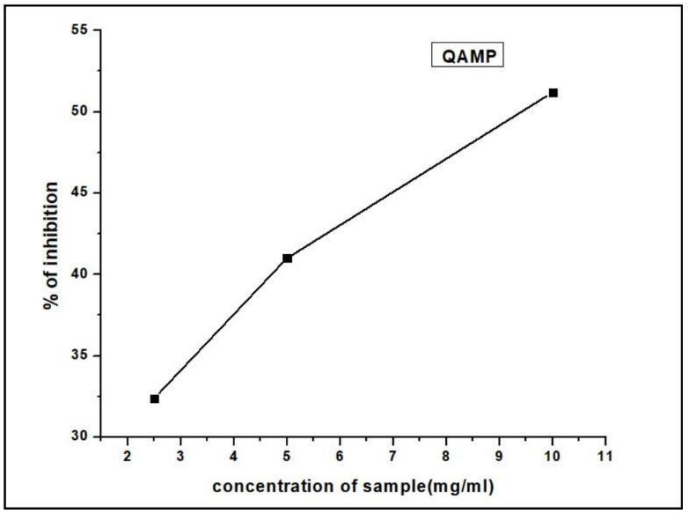


Figure4.18:AntiinflammatoryofQAMP IC_{50}

VALUES OF SCHIFF BASES

IC_{50}represents the concentration at which a substance exerts half of its maximal inhibitory effect. This value is typically used to characterize the effectiveness of an antagonist in inhibiting a specific biological or biochemicalprocess.LowIC50valuemeansthatthecompoundispotentat low concentrations, and thus will show lowersystemic toxicity when administered tothe patient [50].The IC_{50}valuesofQPBA, QANP, QOPD and QAMP are given in the (Table 4.9):

COMPOUND	**IC_{50}VALUES(mg/ml)**
QPBA	1.4978
QANP	1.5147
QOPD	1.4662
QAMP	1.4810
Ibuprofen	2.6817

TABLE4.9:IC_{50}VALUESOFSCHIFFBASES

These IC_{50}values of Schiff bases were compared with ibuprofen a widely used non-steroidal AntiInflammatorydrug. The IC_{50}value of ibuprofen is 2.6817 mg/ml The IC_{50}value ofall the synthesized Schiff Bases are much lower than that of ibuprofen.

Chapter 5

Conclusions

In the present work four new Quercetin Schiff bases were synthesised and characterizedThesearesynthesizedby thecondensationof Parabromo aniline ,2- amino-4-nitrophenol, Ortho phenylenediamine and 2-Amino-4-methylphenol with Quercetin.Synthesizedschiffbasesarecharacterised byIR,UV-visible,H^1NMRand C^{13}NMRspectroscopicmethod.Anti Inflammatory activity of the schiff bases are evaluated.The IC_{50}values of Schiffbaseswerecomparedwithibuprofen awidely usednon-steroidal anti-inflammatorydrug. Fromthe studyQPBA , QANP QOPD QAMPis foundtobeeffectivethanibuprofenandamongthefourschiffbases QOPDismoreeffective forAnti-inflammatoryactivitybecauseofits lower IC_{50}value.

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