Towards Efficient Catalysts *via* Biomimetic Chemistry for Diphenols and Aminophenols Aerobic Oxidation

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ABSTRACT: *Biomimetic chemistry is a new environment-friendly approach that is inspired by biological processes, to produce new catalysts, and to develop 'green' synthetic routes to chemical catalysts based on the benefits of biological systems, aimed to find sustainable solutions to environmental and economic problems. In this paper, we will begin with overviews of two metalloproteins containing copper, which are catechol oxidase and phenoxazinone synthase; this is followed by analysis, and interpretation of some published results in the literature, concerning several attempts to elaborate new catalysts via biomimetic approach for diphenols and aminophenols aerobic oxidation. In order to save the cost of product development, increase efficiency, and eliminate waste; we have presented a theoretical study named Quantitative Structure–Activity Relationship (QSAR) to predict the catalytic activity and physicochemical properties by rational means, with the aim of contributing to the development of the biomimetic approach, and to increase the efficiency of catalysts, by not following leads that are unlikely to be successful.*

KEYWORDS: *Biomimetic approach; Catechol oxidase; Phenoxazinone Synthase; Copper; Catalytic activity.*

INTRODUCTION

Products designer requires improving synthesis processes, in order to limit chemical toxicity, and to reduce the environmental impacts. One of the most attractive approaches to developing chemical processes, in which chemists invent new substances and reactions that imitate biological systems, is "biomimetic chemistry".

The name "biomimetic chemistry" was first used by Breslow in 1972 [1-2]. It's used to describe chemistry that is inspired by biological processes, and to describe rules for the creation of biomimetic materials, to find sustainable solutions to environmental problems; as in the case of plastics with biomimetic properties [3-4], CO_2 photoreduction [5-6], Photochemical degradation of the environmental pollutants: Photocatalysis for the removal of acetamiprid [7], photodegradation of semi volatile organic compounds [8], Photocatalytic degradation of 3-methyl-4-nitrophenol [9], the removal of Sb (III) f rom aqueous solution [10].

In terms of sustainability criteria, biomimetic chemistry has a number of advantages over other synthetic approaches.

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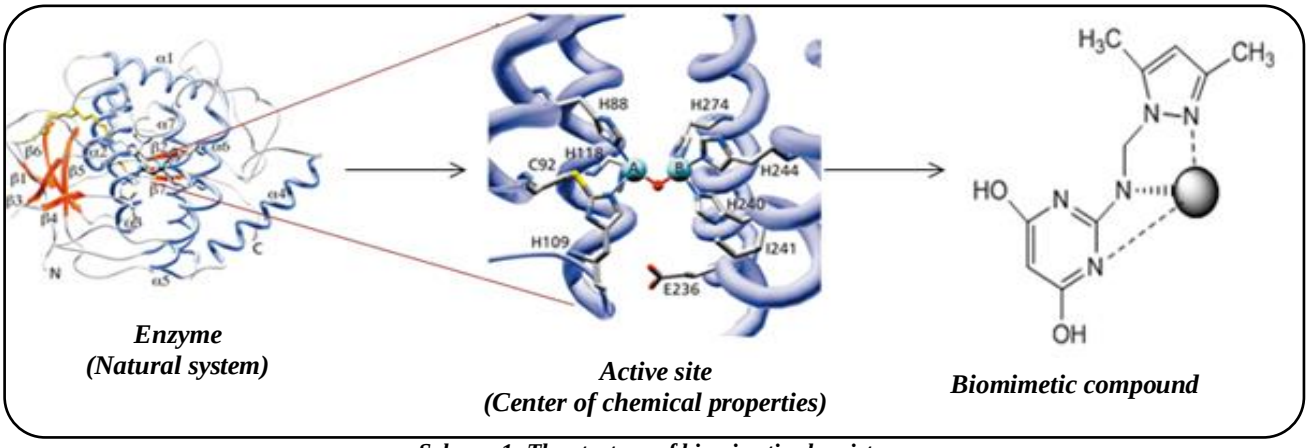


Scheme 1: The strategy of biomimetic chemistry

It is much more energy efficient, does not generate environmental waste, and it is much more selective, thus the yield of the desired reaction is increased [11-12].

On the other hand, biomimetic chemistry leans on biocatalysts, in particular, enzymes and metalloproteins, which have sophisticated, and exceptional catalytic properties, in terms of selectivity and efficiency, and which represent fascinating sources of inspiration.

Biomimetic chemistry transposes especially enzymatic reactions to the organic and inorganic chemistry of synthesis; it involves studying the biological systems, and understanding the processes (structures / mechanisms) implemented at the molecular or atomic scale, and reproducing the structure of the active site of an enzyme by means of the small molecular objects to reproduce the physico-chemical properties of the biological system(structural models) and its catalytic activity (functional models) (Scheme 1).

Moreover with advent of biotechnology, and because the chemical system is easier to handle; the chemical system is used to understand the mechanism of the biological system action.

The advantages and characteristics of biomimetic chemistry have motivated chemists to look into nature systems for inspiration on how to design functional catalysts to investigate different biomimetic reactions.

As with any scientific approach, there are a number of risks. The biomimetic approach also has some limitations, reflected in the lack of reliable information describing the natural system, in particular, because there are few physicochemical analyses of the biological systems to be imitated, thus presenting a problem to the development of biomimetic chemistry.

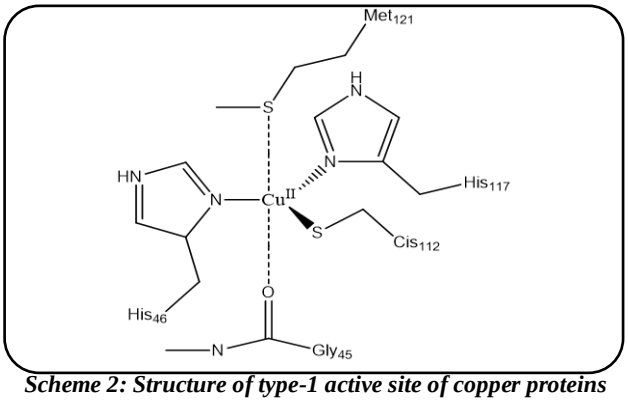
In this review, we are interested to investigate the catalytic activity of some oxidase (oxygenase) metalloenzymes especially copper proteins; which ultimately provide a clue for the development of bioinspired catalysts for the oxidation reactions using air oxygen as the oxidant.

Metalloproteinases containing copper

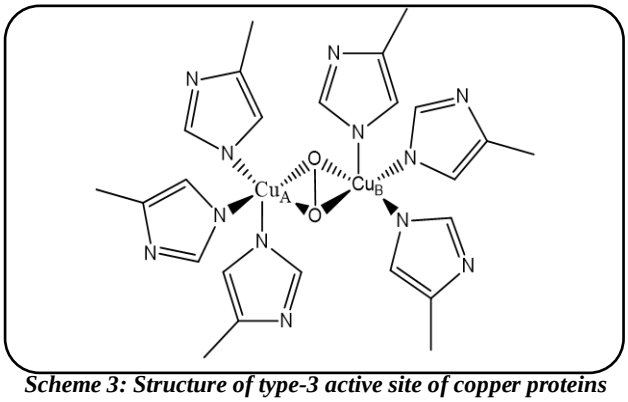
Copper-containing proteins are usually involved as redox catalysts in a range of biological processes, such as electron transfer, dioxygen binding, hydroxylation, dismutation, and oxidation of various organic substrates [13].

Development of the biomimetic catalysts of oxidation, involving copper ion Cu (II) as the active metallic center, has been known as a big challenge in the last decades [14-17], and numerous biomimetic approaches were dedicated to the synthesis of complexes of ion Cu (II) with different organic ligands to reproduce the catalytic activity of biological systems containing copper ion Cu(II) in their active sites [18-19]. These studies aim at imitating the environment of the active site of the enzyme, and better understanding its properties to activate the molecules of dioxygen. The activation of dioxygen is a very important process in biological, and industrial systems [20-21]; this function is often assigned to copper-containing metalloproteins, such as hemocyanin (HC) which transports dioxygen in mollusks and arthropods [22-23], and the tyrosinase (TYR) [24-25] or phenol o-monooxygenase [26-27].

Initially, copper-containing metalloproteins were classified according to their spectroscopic characteristics, which led to the distinguishing of the type-1, type-2, and type-3 active sites containing copper [28].



Scheme 2: Structure of type-1 active site of copper proteins



Scheme 3: Structure of type-3 active site of copper proteins

Type-1 active site

Proteins containing copper, in their active site of type-1, are also called "blues proteins", due to their intense blue color, which is caused by a strong absorption at 600 nm, corresponding to the transition from cysteine sulfur to a Cu (II) ion ($S^- \rightarrow Cu^{2+}$), proteins of type 1 (or T1) have, in their active site, one copper atom, coordinated by two nitrogen donor atoms from two histidine residues, a sulfur atom from a cysteine residue, and a weakly coordinated sulfur atom from, in most cases, a methionine residue [29-30] (Scheme 2).

Type-2 active site

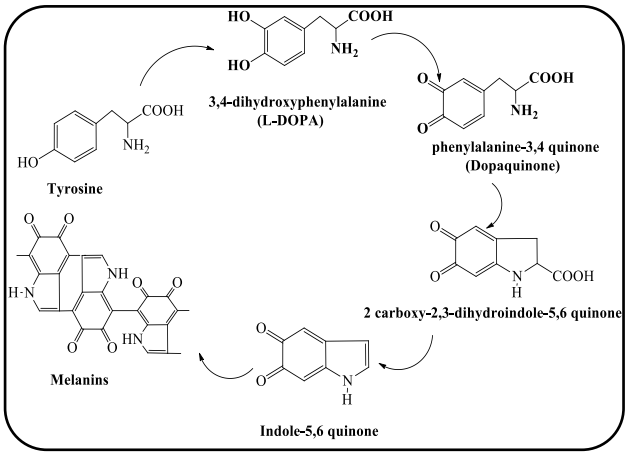
The copper-containing metalloproteins have an atom of copper coordinated by four N and/or O donor atoms in either square-planar or distorted tetrahedral geometry; no atom of sulfur coordinates the copper, thus enzymes have no blue color [13, 31]. Examples of the proteins with this active site include mono-oxygenases. The proteins of this class are mostly involved in catalysis, such as selective hydroxylation of aromatic substrates, C-H activation of benzylic substrates, and primary alcohol oxidation.

Type-3 active site

This site is present in three types of proteins: Hemocyanin (HC), tyrosinase (TYR), and catechol oxydase (CO). This active site contains two copper ions coordinated by three atoms of donors of nitrogen of histidine [31, 32]. A special characteristic of proteins with this active site is their capacity in a reversible way to react with the dioxygen in the ambient conditions (Scheme 3).

Catechol oxidase: Structure and function

Catechol oxidase is a copper protein containing the type-3 active site that catalyzes the oxidation of catechols

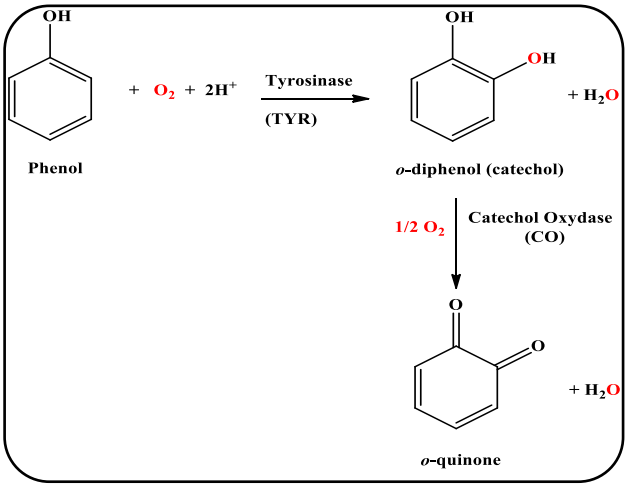


Scheme 4: The Main steps of the melanins formation

(o-diphenols) to corresponding o-quinones that auto-polymerize to produce melanin, which in turn guards damaged tissues against pathogens and insects among many of its protective functions [33-34].

The catalytic process of catechols oxidation to corresponding o-quinones is known as «catecholase activity (CO)", and the catechols oxidation reactions are of current interest due to their wide range of applications in various fields such as the biomedical domain in particular for the determination of the hormonal activity of catecholamines such as the adrenalin, the noradrenaline, or DOPA [35-36] (Scheme 4).

Polyphenols oxidases, and more particularly catecholase (CO) and Tyrosynase (TYR), which are a group of copper-containing enzymes that catalyzes both the ortho-hydroxylation of monophenols (cresolase activity) and the oxidation of o-diphenols to o-quinones (catecholase activity) [37]. Tyrosinase is found in plants, animals, and fungi, and is a common multifunctional copper-containing enzyme. Alive organisms need to do different functions, like the production of melanin for a defensive mechanism against UV radiation [38].



Scheme 5: Oxidation catalysis of the o-diphenol, and the catechol to o-quinone by Tyrosinase and Catechol Oxidase

Reactive and structural characteristics

The oxidation of the o-diphenolics substrates to o-quinones, in the presence of oxygen, is catalyzed by the o-diphenol oxidase activity also called, catecholase (CO). O-quinones are highly reactive compounds, that autopolymerize to produce black, brown or red pigment, generally called melanin, or to react with amino acids and proteins to produce colored compounds [39, 40].

Catechol oxidase was first identified in 1937 [41]. Afterward, it was extracted from a wide range of vegetables and fruits (potato, apple, spinach, and litchi) [42].

In 1999, *Christoph Eicken et al.* [26] determined the structure of catechol oxidase (CO), isolated from sweet potatoes in three different catalytic states: the oxidized Cu(II) containing met form, the reduced Cu(I) containing deoxy form, and in the complex with the inhibitor phenylthiourea (PTU), Fig. 1

Catecholase and tyrosinase biomimetic activities

In recent years, several biomimetic apprto reproduce the catecholase activity; using synthetic chemical materials in order to imitate the environment of the metallic active site of the enzyme, and also better understand its properties to activate dioxygen (O_2).

Recently in 2021, *Murat Tuna et al.* [43] synthesized three copper Schiff base complexes containing hydroxyl functional groups as the model compounds for mimicking polyphenol oxidase (PPO) and peroxidase–like activity (POD).

Enzymatic activities of model complexes were performed spectrophotometrically measuring the increase

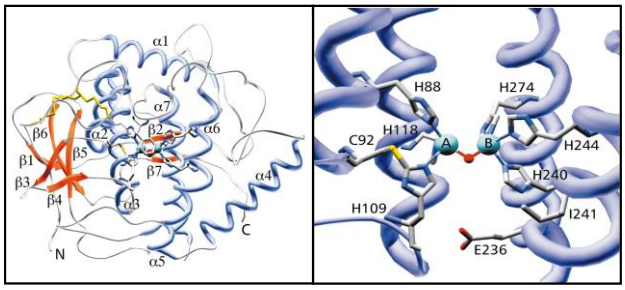
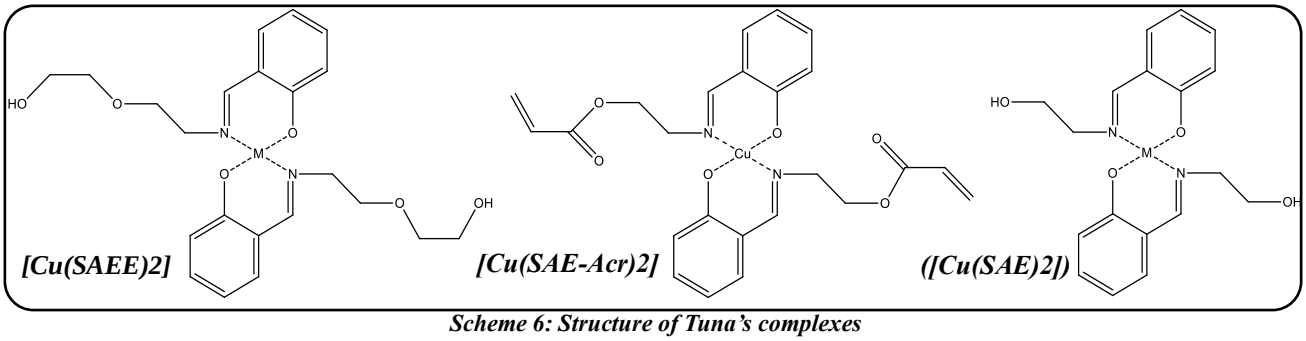


Fig. 1: Active site structure of catechol oxydase by diffraction X-ray [24]

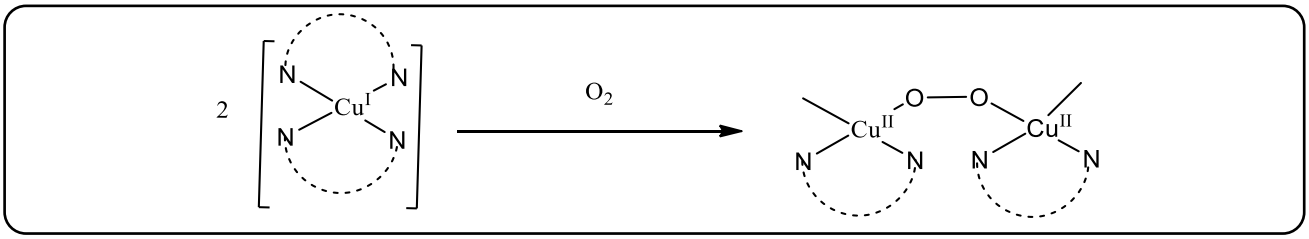
of absorbance at 420 nm for three substrates: 4-methylcatechol, pyrogallol, and L-tyrosine, and the apparent kinetic parameters were calculated based on Michealis-Mentenequation. The results showed that Cu (SAE)2 and Cu(SAE-Acr) 2 compounds had good polyphenol oxidase and peroxidase-like activities, and Cu(SAEE) 2 compound did not show any polyphenol activity at similar conditions, the authors have explained this by the presence of O–H bonds in the free hydroxyl groups of the Cu(SAEE) 2 complex which are weakened by the weak bonds with the other atoms. However, it can also be explained by the absence of one of the mentioned steps in the proposed catalytic mechanism of catechol oxidase; which may be the inability of oxygen to bind between the two copper ions to produce the copper center in the form called oxy (Scheme 7) of the catalytic cycle [44]. The oxy form is prevented by the presence of an oxygen atom in the complex Cu (SAEE)2

In 2020, *Marcos P. Silva et al.* [19] have synthesized two new copper complexes (complex 1 and complex 2) (Scheme 8).

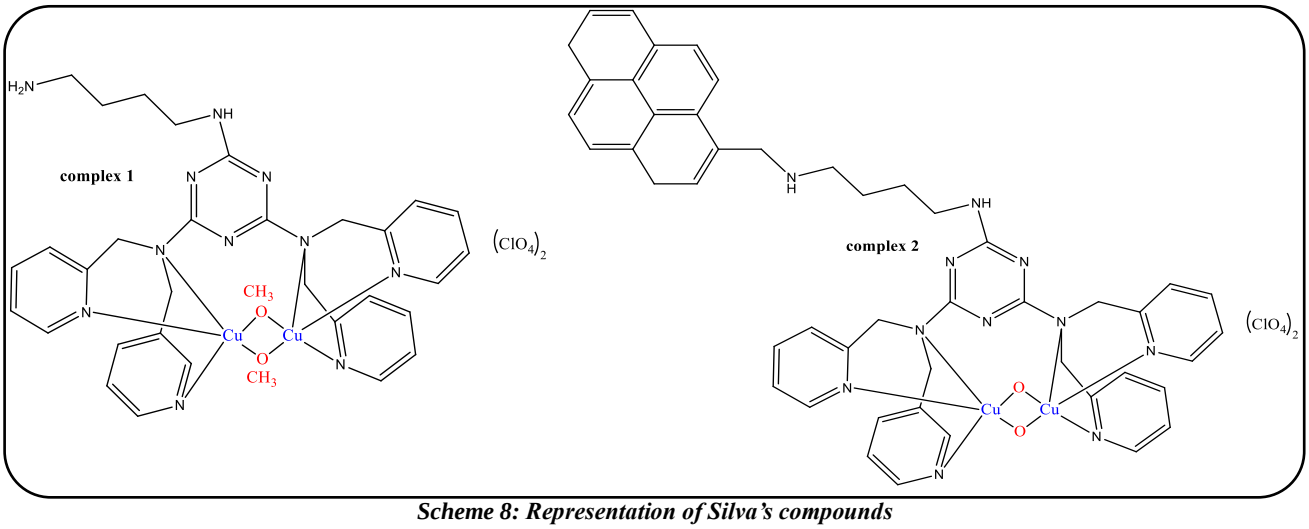
To investigate how modifications of a simple dinuclear copper complex can alter its catalytic activity toward oxidation of the model substrate (3,5-DTBC) to the corresponding (3,5-DTBQ); the catalytic oxidation of substrate was followed by monitoring, spectrophotometrically, the absorbance of the product at 400 nm (ε = 1570 L/cm.mol); and the kinetic parameters was obtained by the non-linear fit of the Michaelis-Menten equation; they found that the studied complexes can be considered optimal functional and structural models for catecholase activity, considering mainly that the values of the catalytic constants obtained are the most effective reported in the literature [45-56]. These chemists have studied the effect of several factors (pH, substrate concentration…) on the catalytic potential of their complexes, they used four



Scheme 6: Structure of Tuna's complexes



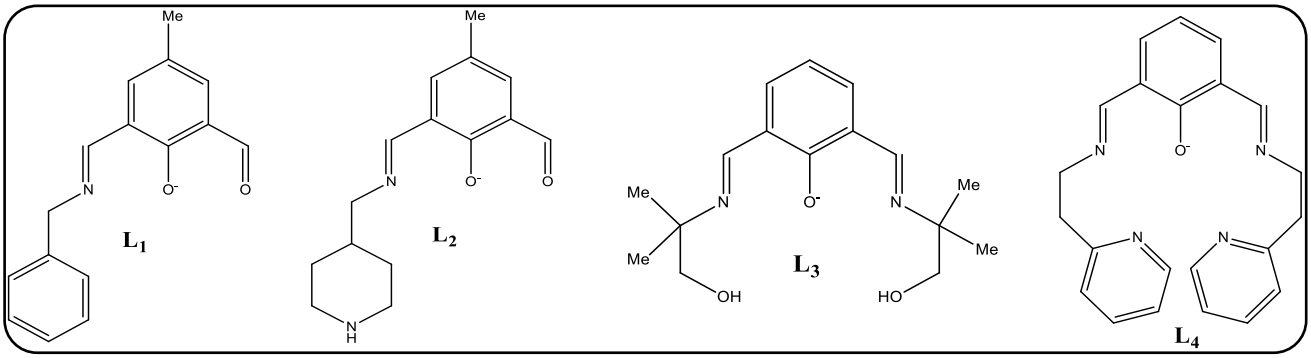
Scheme 7: Formation of copper center in the oxy form proposed in catalytic mechanism of catechol oxidase [44]



Scheme 8: Representation of Silva's compounds

buffers solutions (MES (N-morpholino) ethane sulfonic acid from pH 3.5 to 6.5, HEPES (4-(2-hy-droxyethyl)-1-piperazineethanesulfonic acid from pH 7.0 and 7.5) and CHES (N-Cyclohexyl-2-aminoethanesulfonic acid from pH 8.0 to 10.0) to study the effect of pH, and they found that the optimum pH was 6,5. To highlight the importance of the second coordination sphere for the studied oxidation reaction, new functional groups ((butane-1,4-diamine and pyrene) are inserted in the reaction medium, which favorite the association between the substrate and the catalyst, and appears to be responsible for the significant improvement in the catalysis of the substrate oxidation, this can be explained by the electronic effect exerted by the NH^{3+} group on butane-1,4-diamine, which would contribute to the interaction of the substrate, thus facilitating its coordination to the two copper (II) centers.

In 2012, to understand the key properties of solvents, which have an effect on catecholase activity, *Kazi Sabnam Banu et al.* [57], have synthesized and characterized four new dicopper (II) complexes of phenol-based compartmental ligands L_1-L_4, and studied the catalytic activity of these complexes toward oxidation of 3,5-di-tert-butylcatechol (3,5-DTBC) to produce 3,5-di-tert-butylquionone (3,5-DTB in different solvents (dichloromethane (DCM), methanol (MeOH), methanol-water (50:50, v/v), acetonitrile (ACN) and



Scheme 9: Ligands used in K. S. Banu's study

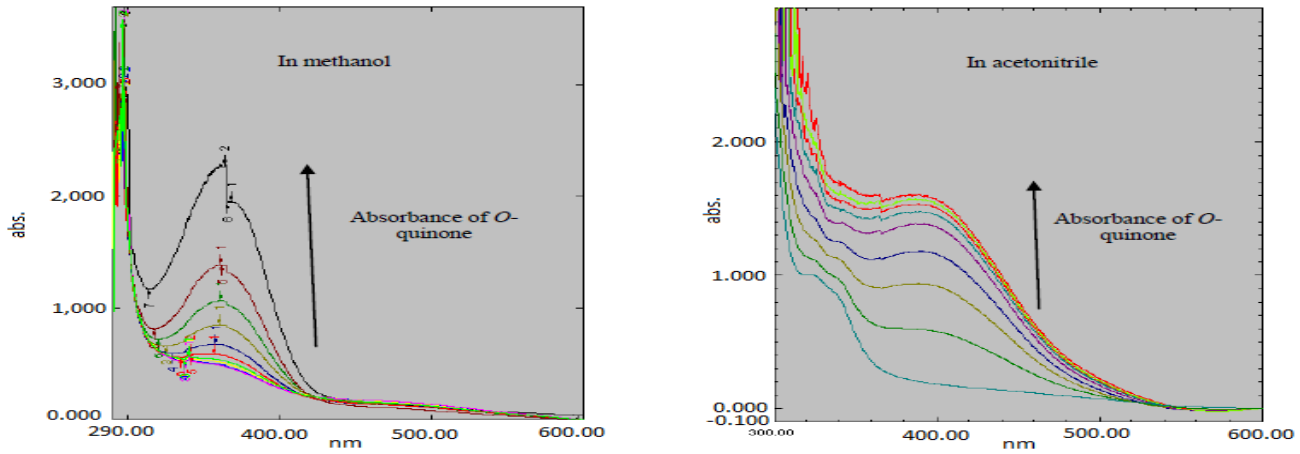


Fig. 2: Increase in the O-quinone absorbance at 390 nm for the combination L_7/$Cu(CH_3COO)_2$ in methanol and acetonitrile [61]

dimethylsulfoxide (DMSO)), They have suggested that the physical parameters of solvents, (dielectric constant, the moment of the dipole, the polarity, etc.), have no significant role in controlling the catecholase of their complexes towards the oxidation of 3,5-DTBC to 3,5-DTBQ, but it is the nature of coordination or solvents that plays the key role in the change of the activity of the complexes, and protic solvents are observed to be a better choice than aprotic solvents for mimicking catecholase activity.

In our turn, and to participate in the development of biomimetic chemistry, we tried to reproduce the catalytic activity of some enzymes (catecholase and tyrosinase) in the laboratory, using complexes that formed in situ based on different types of ligands and metallic salts with studying the effect of many parameters on the catalytic activity of our biomimetic systems. We have estimated the potentialities of several complexes formed in situ arising from pyrazole [58-60], benzyl [61], and Schiff bases [62] ligands and transition metals, in order to develop complexes, which would be very useful as functional model for catecholase and tyrosinase.

Our study indicates that the nature of the ligand, really affects the catalytic activities of corresponding combinations, and the complexes arising from Schiff bases present good results for the oxidation rate which attains 11.52 µmol/L.min as shown in Table 1 [62], this is can be explained by the ease of Schiff bases' reactivity with metal ions. The comparison of rate activity values of the catechol oxidation using different transition metals ions (iron (II), copper (II), cobalt (II), nickel (II)) (Table 2), shows that the copper ion may be the best to produce complexes mimicking catecholase activity. On the other hand, our studies published in the literature [59, 61], demonstrated that the development of biomimetic catalysts was highly dependent on the nature of the solvent; and the protic polar solvents proved to be better than the aprotic polar ones as shown in (Table 3), and the Fig. 2 demonstrated that the absorbance of the o-quinone (product of oxidation reaction of catechol) does not exceed 1,6 after 3 hours of the reaction in the aprotic polar (acetonitrile); but in the protic polar (methanol), the absorbance affects 2 after the same duration.

Table 1: Rate activity of catechol oxidation in methanol based on the type of ligand with $Cu(NO_3)_2$

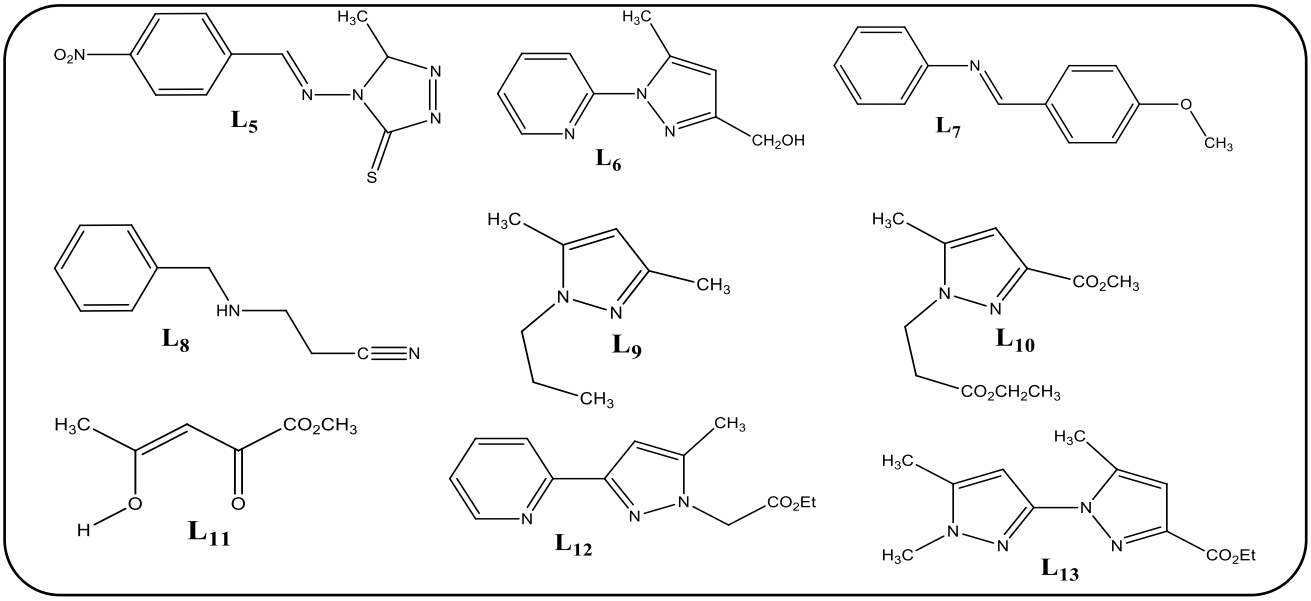
Ligand	Rate activity (µmol/L.min)	References
L_5 (Schiff base)	11,52	[62]
L_6(pyrazole and pyridine based ligands)	0,0022	[59]
L_7 (ligands containing benzyl groups)	3,567	[61]
L_8(electron rich nitrogen based ligands)	0,96	[58]

Table 2: Rate activity of catechol oxidation in MeOH based on the type of active metal (µmol/L.min) [63]

Metallic salt / Ligand	$CuCl_2$	$CoCl_2$	$NiCl_2$
L_9	1,42	0,71	0,53
L_{10}	1,26	0,33	0,24
L_{11}	1,35	0,64	0,26

Table 3: Rate activity of catechol oxidation (µmol/L.min) based on the type of solvent [59]

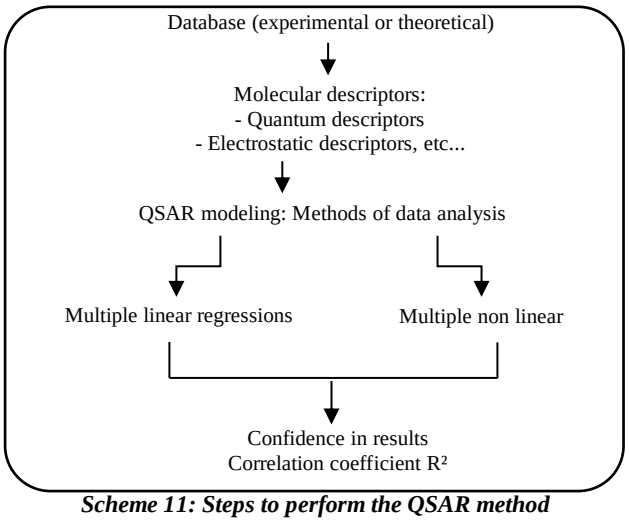
Solvent / Complex	In Methanol (protic polar solvent)	In Acetonitril (aprotic polar solvent)
$L_6/Cu(CH_3COO)_2$	2,7	0,125
$L_{12}/Cu(CH_3COO)_2$	4,37	1,93
$L_{13}/Cu(CH_3COO)_2$	4,44	0,237



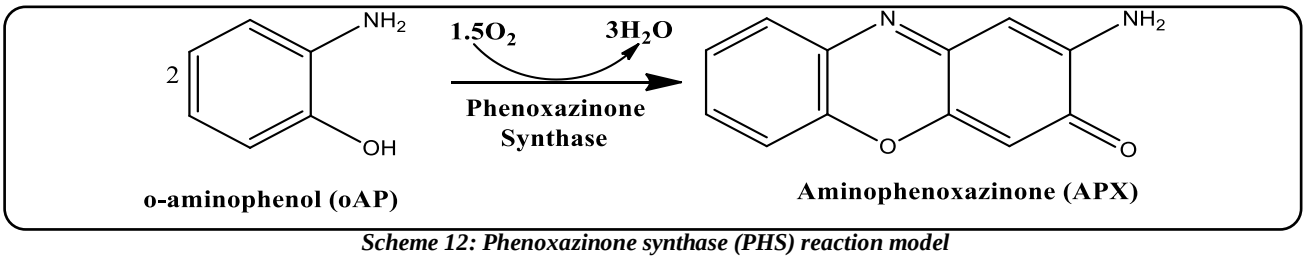
Scheme 10: Structures of tested compounds

Our results allow us to suggest that the best model of catecholase activity is complexes arising from Schiff bases ligands and copper ions in a protic polar solvent.

In continuation of our work in this field, and to understand how a molecular structure brings about a particular effect in a biological system, we have tried to establish the correlation of the electronic and geometric structure with catalytic activity by determining a quantitative relationship between the catalytic activity and the ligand structure, then we are able to form a quantitative structure-activity relationship or QSAR [64], following the principle presented in Scheme 11, to predict catalytic activity and physicochemical properties by rational means, and to comprehend the mechanisms of action within



Scheme 11: Steps to perform the QSAR method



Scheme 12: Phenoxazinone synthase (PHS) reaction model

a series of chemical compounds. This allows us to save the cost of product development, increase efficiency, and eliminate waste by not following leads unlikely to be successful.

Database: The first stage in deriving a QSAR model is to gather and select the molecules representing model compounds of catecholase or phenoxazinone synthase with activity data obtained from the same experimental conditions.

Molecular descriptors: which characterize the molecular structures of the database compounds (energy of the lowest unoccupied molecular orbit (E_{LUMO}). energy of the highest occupied molecular orbit (E_{HOMO}), Electronic chemical potential (μ), Chemical hardness (η)…)

Methods of data analysis: There are several methods to build a model and analyze the statistical data, in order to establish a quantitative relationship between the catalytic activity (catecholase or phenoxazinone synthase activity) and the ligand structure; these methods are available in software such as Excel, Statistica, SPSS, and Multiple nonlinear regressions, Multiple linear regressions…

Confidence in results: finally, the statistical fit of a QSAR can be assessed in many easily available statistical terms, (e.g., the correlation coefficient R^2 between experimental and predicted values for the selected test series); once a model has been developed, predictions of studied catalytic activity can be made for the test set.

Phenoxazinone synthase

Phenoxazinone synthase (PHS) is a pentanuclear copper oxidase that catalyzes the oxidative coupling of two molecules of substituted o-aminophenol to produce phenoxazinones in the last step in the biosynthesis of the antibiotic actinomycin-D [65], which is medicinally very important for the treatment of different kinds of tumors [66-67].

Phenoxazinone synthase was first isolated from Streptomyces antibioticus in 1962 by Katz and Weiss back [68-69]; but its structure was unknown until 1993 with the advent of John C. Freeman and coworkers [70], presenting spectroscopic studies, which have suggested that the phenoxazinone synthase contains one type 1 copper center, with the remaining copper atoms bound as type 2 copper centers. The spectrum in these studies does not show the presence of type 3 copper centers. In 2006, *Alex W. Smith et al.* [71], have determined the structure PHS using X-ray diffraction to a resolution limit of 2.30 Å, and reveals that PHS is known to be active in two oligomeric forms with distinct catalytic activities: low-activity dimers and high-activity hexamers; the structure of hexameric PHS shows the presence of five copper atoms, including the presence of type 3.

In literature, numerous studies were dedicated to the synthesis of biomimetic functional models of phenoxazinone synthase, these studies aim to mimicking the environment of the metallic active site of the enzyme and also better understand its properties of activating molecular oxygen.

W.P. Sohtun et al. (2021) [72] have synthesized and characterized a series of new copper (II) complexes based on N_3O tripodal ligand scaffolds, to produce biomimetic models for phenoxazinone synthase; using 2-aminophenol oxidation into 2-aminophenoxazine-3-one, as a model reaction, in the presence of dioxygen, they found that catalytic activity is strongly influenced by the electronic and steric factor of the ligands; the oxidation kinetics was followed by the spectroscopic method by recording the absorbance of the product at 430 nm. Kinetic parameters (Michaelis binding constant (K_m), Maximum reaction velocity (V_{max}), and turnover number ($K_{cat.}$)) of phenoxazinone synthase-like activity were calculated by Michaelis–Menten type kinetic studies; it showed that the first-order reaction kinetics at lower concentrations and the saturation kinetics (zero-order) observed at higher substrate concentrations. In order to find parameters influencing the activity catalytic of studied complexes, these scientists have calculated the steric maps and percent

Table 4: The K_{cat} values of o-aminophenol oxidation in methanol (MeOH) based on the type of active metal

Ions complexes used in catalyst formation	K_{cat} (h^{-1})	References
Fe(III)	$1,96.10^2$	[74]
	$3,23.10^2 – 5,25.10^2$	[75]
Co(III)	$45,9.10^2$	[76]
	$97,2.10^2$	[77]
	$3,33.10^2$-$5,71.10^2$	[75]
Mn(II)	$3,15.10^2$	[78]
	$0,082.10^2 – 0,26.10^2$	[79]
Cu(II)	$3,60.10^2$	[80]
	$10,65.10^2$	[55]
	$3,40.10^2$	[81]
	1210.10^2	[82]

buried volume (% V_{bur}) for their complexes, they find that the steric and electronic nature of the ligands, affect the catalytic activity, and the complexes with less steric and more electron-withdrawing groups showed the highest catalytic activity as compared to the sterically crowded ligands.

Saikat Banerjee et al. (2020) [73] have synthesized and characterized a new complex based on Mn(II) using N_2O_4 donor Schiff base ligand, by examining the catalysis of oxidation of o-aminophenols, they found that their complex's efficient functional model for phenoxazinone synthase. The progress of the oxidation reaction was monitored by the successive increase in the absorbance band of the product at 420 nm.

Different kinetic parameters like V_{max}, K_M, and K_{cat} were also determined by linearization of Michaelis–Menten equation, to be $K_M = 1, 09.10^{-2}$M, Vmax = $6, 14.10^{-8}$M/s and $K_{cat} = 22,1h^{-1}$

The comparison of the results presented in the works above of *W.P. Sohtun et al.* (2021) [72] and *Saikat Banerjee et al.* (2020) [73], allows us to suggest that copper ion may be the best ion to reproduce the phenoxazinone synthase activity; this is confirmed by K_{cat} values calculated in the two studies. Recent works in this area of mimicking the function phenoxazinone synthase, using some transition metals complexes suggest that copper may be the best choice to produce the best model of PHS; this is confirmed by the K_{cat} values of o-aminophenol oxidation of some transition metals presented in table 4. The results collected in Table 5, show that the nature of solvent has a significant effect on the catalytic activity of phenoxazinone

Table 5: The K_{cat} values of o-aminophenol oxidation by some Cu(II) complexes based on the type of solvent (in methanol (MeOH) and in acetonitrile (CH_3CN))

Ions complexes used in catalyst formation	K_{cat} (h^{-1})	References
Cu (II) In acetonitrile (CH_3CN)	$2,36.10^2$	[80]
	$2,13.10^2$	[55]
	$0,111.10^2$	[83]
Cu (II) In methanol (MeOH)	$3,60.10^2$	[80]
	$10,65.10^2$	[55]
	$3,40.10^2$	[81]
	1210.10^2	[82]

synthase models, this can be explained by the coordination power or protic nature of the solvents; the protic and polar solvent (like methanol), appears a better solvent to reproduce phynoxazinone synthase activity, than the aprotic and polar solvent (like acetonitrile), this solvent effect has already been studied in one of our work in 2013 on the catalytic activity biomimetic models of catecholase [59].

Catalytic promiscuity of biomimetic models of Catecholase and Phenoxazinone synthase

Catalytic promiscuity is the ability of enzyme active sites to catalyze multiple chemical transformations [84], in living systems, many enzymes show catalytic promiscuity and participate in many different types of reactions, such as Dizinc Aminopeptidase [85], Chymotrypsin [86]. In literature, catalytic promiscuity of many biomimetic models is reported and exploited in numerous synthetic applications; among these examples, many chemical models of Catecholase have been verified to be able to catalyze the oxidation of o-aminophenol to produce phenoxazinones (Phenoxazinone synthase) [87-91]. Increased knowledge of the catalytic promiscuity of chemical model, allows understanding of the mechanistic pathway of Catecholase and phenoxazinone synthase activity, and good exploitation of the catalytic activities of one chemical model for the catalysis of several reactions.

CONCLUSIONS

In this review, we have presented a biomimetic approach to catalytic processes, in order to contribute to the scientific advances of catalysis and to reproduce new efficient catalysts by following environmental-friendly pathways that are likely to be successful. Our study is based on analysis, and interpretation of some published

results in the literature, especially that focus on biomimetic functional models of catechol oxidase and phenoxazinone synthase, the two enzymes which catalyze the oxidation of ortho-diphenols, and the coupling of 2-aminophenols, respectively. As shown by the literature studies presented in this review, the nature of the ligand, really effect the catalytic activities of functional models of catechol oxidase and phenoxazinone synthase, and the complexes arising from Schiff bases present good results, in the protic and polar solvent (like methanol), and copper appears a better ion to produce the best model of the two studied enzymes.

In our point of view, it must be said that biomimetic chemistry has taken a great importance in the catalysis field, and to take full advantage of their benefits, and to save the cost of product development, we propose some solutions to follow a biomimetic approach that is likely to be successful in catalysis:

- Synthesis of ligands that may exhibit physicochemical properties of the active site of the enzyme studied by resembling the same type of atom of this active site involved in the complexation of metal ions.
- Model catalysts must contain the same active site metal ion
- Development of theoretical studies that allow us to predict the studied activities and physicochemical properties by rational means.

On the other hand, biomimetic chemistry must take its place in the field of materials; the challenge of biomimetic chemistry in this field is to replace the processes based on the use of rare raw materials, difficult to extract and purify, with processes operated under conditions of mild chemistry; in order to generate multifunctional, biodegradable, mechanically stable materials, and the decomposition and recycling of which are always ensured.

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