Role of Catalysis and Catalytic Agents in Drug Stability

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Abstract

Catalysis is the phenomenon of an increase in the rate of reaction with the addition of any external chemical/biochemical substance (i.e., catalyst). These external substances (temporary intermediate) in the chemical reactions/biological processes provide an alternative pathway with lower activation energy. Catalytic agents help in the lowering of the energy of the reaction to reach the transition state with no change in the free energy from the formation of reactants to the final products. These catalytic agents help in the speeding up of chemical reaction/biological process and also help in the production of some important pharmacologically active compounds for the treatment of many ailments. Drug discovery is the foundation of development in the healthcare system. Multiple techniques and methodologies have been adopted to achieve the balance drug molecule. However, functionally catalytic agents performed a novel mechanism in the field of drug discovery and stability. Stability continues to impact on the drug discovery and development greatly. New catalytic agents (i.e., organometallic enzymes, engineered genes, transition metal, and their salts) have been developed to accelerate the growth and development of stable compounds. The catalyst works by opening up a route between starting material and product with a lower activation barrier than the un-catalyzed process. This chapter gives detailed information to understand the catalysis, types of catalysis, the effect of catalytic agents on drug discovery, and the stability of drugs and drug substances.

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8.1 Introduction

Catalysis shows a significant role for the benefit of mankind and its role to develop a connection between science and technology with worldwide development and modernization. Different industrial development based on the catalysis process because over 90% of products have been originating depends somewhat on the catalytic process such as chemical, agriculture, polymer, petroleum, and pharmaceuticals [1]. The benefits of the catalytic process include cost minimization, time effectiveness, and reduced waste formation to make it an environmentally safe and sustainable manufacturing process. Catalysis is based on green chemistry principles [2]. Catalysis provides a helpful tool in smart synthetic design in which we obtained high value product output with simpler methods, therefore improvising the various industrial manufacturing processes. The significance of catalysis is valued by honoring Nobel Prizes in various fields of chemistry in the last 40 decades. These include the revolutionary efforts in polymers by Ziegler and Natta (1963); the remarkable work on organometallic compounds by Wilkinson and Fischer (1973); the hydrogenation and oxidation approaches of Knowles, Noyori, and Sharpless (2001); the award given to Chauvin, Grubbs, and Schrock (2005) for metathesis; the latest acknowledgment on cross-coupling reactions of Heck, Negishi, and Suzuki (2010); and many more [3].

The catalytic reaction is a cyclic process as catalyst takes part in the reaction and is available in its original state after reaction and could be used again and again in other reactions. A catalyst speeds up a chemical reaction by making an intermediate with the reactants and enables them to form a product [4]. The process of accelerating the speed of any reaction caused by the addition of a substance is termed as catalysis [5]. Catalysts speed up the chemical reactions by providing another pathway during the reaction having lower activation energy than a chemical reaction that proceeds in the absence of a catalyst [6], whereas a substance which decreases the speed of a chemical reaction is termed as an inhibitor rather than a catalyst [5].

8.1.1 Unit of Catalytic Activity

Catalytic activity (CA) is typically symbolized by "z" and calculated in mol/s, which is in SI unit termed as "Katal" (1 kat is equivalent to 1 mol/s). One katal is the amount of catalyst, i.e., one mole of catalytic agent and reactant is converted into the final product in one second. The catalyst productivity could be measured by the turnover number (TON) which is measured in one second and CA is calculated as turnover frequency (TOF) [7].

8.2 Working Principle

Catalysts typically react with more than one reactant in a chemical reaction to generate intermediates that convert into final product by recovering the catalyst at the end of reaction [8]. The classical representation of a reaction scheme is described here, where ***C*** is the catalyst, A and B are reactants, and Z is the final product (Eqs. 8.1, 8.2, 8.3, 8.4, and 8.5):

$$\mathrm{A} + C \rightarrow \mathrm{A}C \tag{8.1}$$

$$\mathrm{B} + \mathrm{A}C \rightarrow \mathrm{AB}C \tag{8.2}$$

$$\mathrm{AB}C \rightarrow \mathrm{C}Z \tag{8.3}$$

$$C\mathrm{Z} \rightarrow C + \mathrm{Z} \tag{8.4}$$

The catalyst is utilized at the beginning of a reaction (Eq. 8.1) but is recovered at the end of chemical reaction (Eq. 8.4), so it is not represented in the overall equation of the reaction:

$$\mathrm{A} + \mathrm{B} \rightarrow \mathrm{Z} \tag{8.5}$$

8.3 Reaction Energetics

The reaction energetics in the catalyzed reaction is based on difference in the transition states and by lowering the activation energy. When molecular collisions are increased during the chemical reaction, the energy requirement is also increased to attain the desired transition state. Therefore, catalyst facilitates the process of chemical reaction which might be blocked or slowed down due to the kinetic barrier. So, it can increase the rate of reaction or proceed the chemical reaction at lower temperature [9]. The catalyst may also stabilize the transition state as well as cause reduction in the kinetic barrier by lowering the energy levels difference between reactants and their transition state. This reaction energetics can be explained by using the energy profile diagram (Fig. 8.1) [6].

8.4 Types of Catalysis

The two major types of catalysis are heterogeneous and homogeneous catalysis, which are described below.

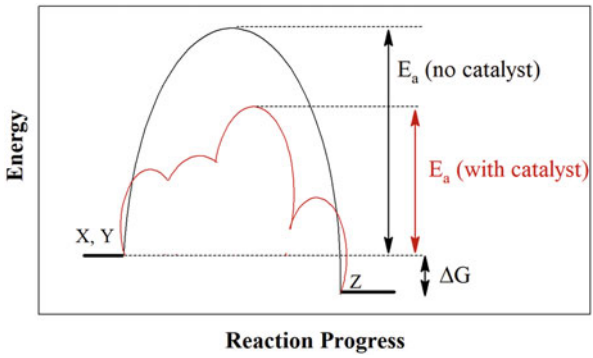


Fig. 8.1 Reaction energetics in the presence and absence of catalyst

8.4.1 Heterogeneous Catalysis

In heterogeneous catalysis, catalysts exist in a different phase than the reactants. Catalysts used in heterogeneous catalysis are solid and able to participate in a chemical reaction where substrates are in a liquid or gaseous phase. The mechanism of heterogeneous catalysis is based on surface phenomenon, i.e., adsorption [10]. This is a cycle of molecular adsorption, reaction, and desorption occurring at the catalyst surface. The surface area of heterogeneous catalyst plays a vital role on the speed of chemical reaction. The active sites present on the heterogeneous catalyst may be either a planar metal surface or a crystal edge or a complicated combination of these two. Some studies on heterogeneous catalysis for various pharmaceutical compounds include enhanced ibuprofen (IB) removal by heterogeneous-Fenton process over Cu/ZrO_2 and Fe/ZrO_2 catalysts [11]; base metal–catalyzed hydrogen isotope exchange [12]; heterogeneous copper-catalyzed C–S coupling via insertion of sulfur dioxide [13]; shape-controlled metal nanocrystals [14]; catalytic ozonation of diclofenac (DF), sulfamethoxazole (SM), and 17α-ethynylstradiol in the presence of a commercial γ-Al_2O_3 and a synthesized Co_3O_4/Al_2O_3 catalyst [15]; oxidation treatment of fluoroquinolone using TiO_2 [16]; synthesis of deuterium-labeled drugs by hydrogen–deuterium (H–D) exchange [17]; furan synthesis [18]; and palladium-derived catalysts in the synthesis of fine chemicals, pharmaceutical intermediates, and active pharmaceutical ingredients [19].

8.4.2 Homogeneous Catalysis

Homogeneous catalysts worked on the same mechanism as in heterogeneous catalysis. In this type of catalysis, the reactants are mostly in liquid phase/system. Homogeneous catalysis is frequently indistinguishable with the process of organometallic catalysis [20]. Usually, organic catalysis needs a higher amount of catalyst (per % mol of reactant) as compared to transition metal catalysis where catalysts are available in major quantities to reduce the cost of the entire process. Homogeneous catalysis is more efficient as it is highly selective in specific product formation,

enhances catalytic activity, and generates heat if required in case of exothermic reactions and the characterization of species because of the reaction is in the same solution/phase. Some examples of homogenous catalysis are perovskite catalytic ozonation of diclofenac and 17α-ethynylestradiol [21], formation of alkylaldehyde by hydroformylation with alkene and carbon monoxide, formation of methyl acetate by esterification of carboxylic acids [22], and application of homogeneous catalysis in supercritical fluids [23]. Homogenous catalysis is of different types (i.e., general acid and base catalysis, Diels-Alder reactions, thiazolium ions in cannizarro reactions, epoxidations, hydroxylations and polyester condensations). However, among them, the general acid–base catalysis is of greater implication in the discovery and stability of pharmaceutically active compounds; this is discussed below.

8.4.3 General Acid and Base Catalysis (Ester Hydrolysis)

Acids (Lewis acids) and bases act as powerful catalysts for a variety of chemical reactions, in the laboratory, industry, and processes occurring in nature. Historically, catalytic action was regarded as one of the essential characteristics of acids. However, in the nineteenth century, the parallel occurrence of catalytic action and electrical conductivity was one of the important evidences in establishing the theory of electrolytic dissociation as the basis of acid–base catalysis [24].

Acid–base catalysis was initially unknown and considered as an influence of acid or base on the catalysis. However, it is now believed that acid–base reaction is in between the catalyst and reacting substance (substrate). Nowadays, the knowledge of reaction mechanisms is sufficient to suggest detailed sequences of reactions for acid or base catalysis. In most acid–base reactions, the addition or removal of a proton does not bring about any drastic change in the structure of the molecule or its stability or reactivity. However, the addition or removal of a proton may result in the instability of substrate (due to decomposition or rearrangement) and reactivity toward some other species present in the system. In cases of rearrangement, the regeneration of the catalyst often involves the removal or addition of a proton at a site other than that at which the initial addition or removal took place. It is not necessary that the substrate in an acid- or base-catalyzed reaction should itself have marked acid–base properties, since even a very small extent of initial acid–base reaction may be enough to bring about the subsequent change [25, 26].

8.4.4 Other Types of Catalysis

Some other types of catalytic processes which are initiated with external stimuli (i.e., light, heat, etc.) or by the influence of non-catalytic agents are described below.

8.4.5 Photocatalysis

Photocatalysis is the catalysis in which the catalyst is activated by light (i.e., UV or visible light). The photoactivation of reactants results in the transformation from the ground state into excitation states through intersystem crossing (ISC). Therefore, this activation results in a series of chemical cascades that could not be possible without photoactivation of reactants. Through this phenomenon, the molecular oxygen ($^3O_2$) is converted into singlet oxygen ($^1O_2$) and widely used in photodynamic therapy (PDT) [27]. Few examples of photocatalytic reactions include removal of cytotoxic drugs from wastewater [28], antibacterial activity of metal oxide nanomaterials (NMs) [29], degradation and inactivation of tetracycline by TiO_2 [30], degradation of lincomycin (LM) in aqueous medium [31], titanium dioxide photocatalysis [32], and water purification by semiconductor [33].

8.4.6 Biocatalysis

Biocatalysis may be either homogeneous or heterogeneous. Soluble enzymes work on the principle of homogeneous catalysis and some of membrane-bound enzymes are categorized as a heterogeneous catalyst [34]. Screening of biocatalyst may be carried out by various instrumental techniques, i.e., chromatography, capillary electrophoresis, mass spectrometry, etc., through absorption or emission of light as the reaction proceeds [35]. Some monoclonal antibodies behave as a weak catalyst by lowering its activation energy in chemical reactions where the binding target is stable [36, 37]. The advancement in the designing of the biocatalyst is achieved through rational selection and mutation by recombinant DNA technology which facilitates the production of the process-compatible enzymes [38].

8.4.7 Nanocatalysis

The fabricated NMs that are used to accelerate the chemical reactions are termed as nanocatalyst and the phenomenon is known as nanocatalysis. Studies have been reported on the catalytic effect of nanocatalysts in different reactions [39]. Examples of nanocatalysis are the effect of gold nanocatalysts in the detection of mefenamic acid (MA) in pharmaceutical preparations [40] and selective transfer of hydrogen in functionalized nitroarenes using cobalt-based nanocatalysts [41].

8.4.8 Tandem Catalysis

Tandem catalysis is generally categorized under the homogeneous catalysis. In this catalysis, multiple catalysts are involved in a chemical reaction to form a product [42]. A porphyrin porous organic polymer with bicatalytic sites for highly efficient one-pot tandem catalysis [43], asymmetric coupling of ethylene and enynes to

functionalized cyclobutanes [44], direct catalytic synthesis of imines from alcohols using manganese octahedral molecular sieves [45], and homo- and heterodinuclear complexes with triazolyl-diylidene [46] are some examples of tandem catalysis.

8.4.9 Autocatalysis

Autocatalysis is the process in which the catalysts are formed during the reaction as an end product which accelerates the chemical reaction in the forward and backward direction [47, 48]. Formose reaction [48], autocatalytic degradation of obidoxime [49], and controlled autocatalytic nitration of phenol in a microreactor [50] are a few examples of autocatalysis.

8.5 Importance of Catalytic Agents in Drug Discovery and Stability

Drug discovery involves the learning of scientists about the dysfunction of biological targets (i.e., receptors, enzymes, proteins, genes, etc.) which are directly involved in the biological process. The development of a new drug produces a novel mechanism of action which is entirely different from the priorly approved drug for any ailments indicating the importance of drug discovery. Medicines with some modifications are more efficient in the domain of potency, safety, tolerability, and convenience (i.e., palatability, reduction in frequency, fixed-dose combination (FDC), reduction in the cost of therapy and hospitalization) [51].

Stability is the most important attribute of drug discovery and for potential compounds used in the treatment of diseases. The instability of the drug leads to the degradation that may cause rejection of compound in a later stage of development and would cause some major problems in the biological system. The importance of stability studies in drug discovery is to recognize responsive chemotype, important lead series, to detect precise structure–activity relationship (SAR) due to degradation, to improve stability by structural modification, and to elucidate the mechanism of action [52].

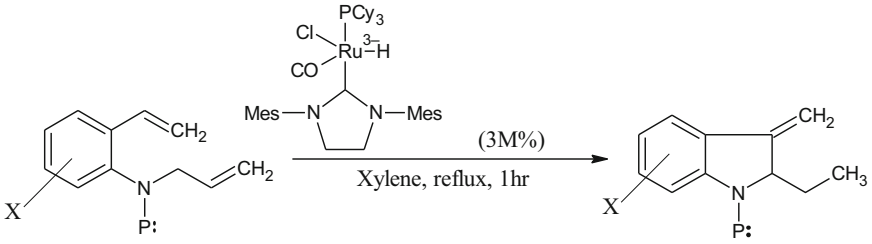
8.5.1 Challenges in Drug Discovery

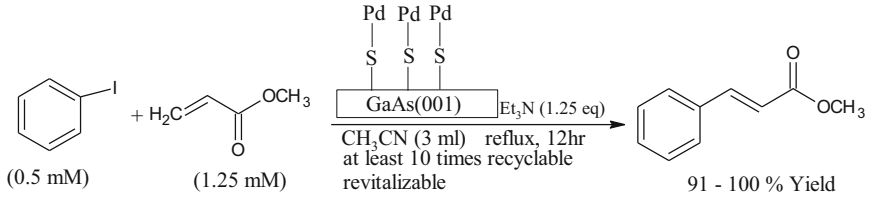
Nowadays, the basic problem in drug discovery is the increasing rate of failure in clinical trials, due to the problems associated with inappropriate pharmacokinetics, poor efficiency, and high toxicity. However, different strategies have been adopted to minimize the risk of failure in drug discovery. To find a better drug profile, it is important to determine the absorption, distribution, metabolism, elimination (ADME), and toxicity pattern as well as activity and selectivity of the drug molecule. To accelerate the drug discovery, significant improvements have been made by adding few novel techniques such as polymer-assisted solution-phase synthesis

(PASPS), microwave-assisted organic synthesis (MAOS), continuous flow process as well as ultra-performance liquid chromatography (UPLC), and supercritical fluid chromatography (SFC) for the improvement of an analytical profile of the drug molecule [53].

8.6 Role of Catalysts

Currently, the fundamental development in organic chemistry is organometallic catalyzed carbon–carbon bond formation and its application in medicinal and process chemistry. The discovery of two novel organometallic catalysts is ruthenium hydride with a nitrogen-containing heterocyclic carbine (Eq. 8.6) [54] and organopalladium catalyst supported on a sulfur-terminated semi-conductor gallium arsenide (001) (Eq. 8.7) [55]. The most important factor is the benign nature of both the catalyst as they generate indole derivative with sufficient atom density and increases catalysis by tenfold in Mizoroki–Heck reaction with an only trace amount of leached palladium. Ruthenium carbine catalysts used in the synthesis of biologically active natural products, due to their stability, functional group tolerance, easy handling, and commercial availability. Identification of the real catalyst is one of the critical elements in the development of a novel heterogeneous catalyst [56].





8.6.1 Catalytic Role of Metal Ions

The most important and innovative catalytic role of Zn-dependent histone deacetylase 8 (HDAC8) is to remove acetyl moieties from histone tails, which generally regulate transcriptional repression and gene silencing due to the closed chromatin structure. The catalytic process of Zn-dependent HDAC8 is of high importance as it shows novel development in antineoplastic agents. Previously in 2006, FDA (Food and Drug Administration) accepted SAHA (suberoyl + anilide + hydroxamic acid) as an anticancer drug which is directly combined with catalytic Zn ion and HDAC inhibitor [57].

8.6.2 Organometallics Catalysis

Organometallic enzymes play a pivotal role in drug discovery and development. The natural enzyme (hydrogenase) and artificial enzyme (metalloenzyme) represent the novel innovation in drug discovery [54]. The inhibition of carbonic anhydrase metalloenzyme plays a pivotal role in the development of anti-cancerous, anticonvulsant, and anti-glaucoma drugs. Metalloenzyme carbonic anhydrase also possesses the potential to develop anti-infective drugs (anti-fungal and anti-bacterial agents) [55]. Among solid catalysts, metal oxides have been considered as the most important as well as extensively utilized category. Mixed metal oxides represent mainly in heterogeneous catalysis and widely employed in the academic research, chemical, and pharmaceutical industries. Transition metals, among the metal oxide catalysts, played an important role extensively due to several advantages, i.e., selective action, easy regeneration, and low cost of production. They are used in different important reactions which include isomerization, oxidation, dehydration and dehydrogenation, etc.

The mixed metal oxides are widely used in different fields, especially in catalysis and organic synthesis. Mixed metal oxides played a vital role in catalysis and in the field of organic synthesis with the fundamental application in drug discovery [58]. Metal salts (e.g., CuCl, $AuCl_3$, $Pd(OAc)_2$) have been widely used for the catalytic processes that eventually discover many different reactions and become a part of organic synthesis. This leads to the formation of catalysts with improved reactivity, selectivity, high level of purity, and a minimal amount of waste material. The tunability and modularity of ligand trait in catalyst functioning can be beneficial for the development of novel entities [59]. The two most impactful and transformative fields of chemistry are organometallic and catalytic chemistry. Drug discovery and material synthesis and its transformation are the major achievements of these disciplines. It has been found that catalysts containing transition metal complexes are the most successful candidates in the field of drug discovery and stability [60].

8.7 Factors Affecting Stability

There are many factors that affect the stability of the drug candidate. Instability may lead to the incorrect bioassay, erroneous SAR's, false-positive high-throughput screening (HTS) hits, low bioavailability, as well as drug withdrawal. Some of the factors which influence the stability of drug are briefly discussed below:

8.7.1 Effect of pH

pH plays a vital role in the stability of pH-dependent compounds. Some compounds are stable at neutral conditions whereas others are stable under acidic or basic conditions [25]. Different studies have been carried out on the effect of pH as a function of stability on different drugs (i.e., riboflavin (RF) [61], cyanocobalamin (CY) [62], levofloxacin (LV) [63], and moxifloxacin (MF) [64]. It has been found that the stability of the drug moiety is dependent on the ionic state (anion, zwitterion, cation) and susceptibility toward H^+/OH^--catalyzed hydrolysis.

8.7.2 Effect of Concentration

Degradation of certain compounds directly depends on the initial concentration of drug and with the interacting substance (counterion) present in the system. Stability can be determined with a variety of counter ions (i.e., excipients, buffer components, sensitizers, etc.). A suitable buffer at a particular pH should be selected to achieve optimum stability. Degradation rate can be increased with the higher counter ion concentration. Degradation of various drugs (i.e., cefaclor (CF) [65], RF [66–68], etc.) under the influence of buffer has also been reported in several studies.

8.7.3 Effect of Ionic Strength

The ionic strength of buffer can affect the stability of certain drugs i.e., RF [69], gonadorelin [70] and indomethacin [71]. It alters the pK_a and activity of coefficient (enthalpy change) which accelerates acid or base catalysis.

8.7.4 Effect of Co-solvents

Co-solvents may produce unwanted effects on stability by changing the dielectric constant of the medium which may lead to the degradation or enhanced stability of drugs (i.e., azathioprine (AZ) [72], RF [73], thymoquinone (TQ) [74], etc.).

8.7.5 Effects of Protein Binding

The addition of protein can reduce the rate of hydrolysis, owing to protein binding and reduction of free-drug concentration. Bound drug molecules RF [75], roscovitine [76], are not fully accessible to acid- or base-mediated hydrolysis. It has also been demonstrated that stability at pH 7.4 was improved with the addition of serum protein (4%) for a set of carbonate esters and phenylacetate [77, 78].

8.7.6 Effect of Light

Some drugs are sensitive to light (i.e., UV (180–380 nm), visible (380–780 nm)) and its exposure results in the enhanced degradation/decomposition (i.e., RF [61], cyanocobalamin [62], difloxacin (DF), and sarafloxacin (SF) [79]). Photosensitive drugs in aqueous medium or solid dosage form are susceptible to the degradation which results in the toxicity to biological system. Photodegradation reactions of drugs depend on the type of reaction initiated by light i.e., photooxidation (e.g., AA), photoreduction (e.g., RF), photoaquation (e.g., CY), photocyclization (e.g., meclofenamic acid (MA)), photodealkylation (e.g., chloroquine (CQ)), photodecarboxylation (e.g., amino acids), photoisomerization (e.g., aztreonam (AZ)), photodimerization (e.g., primaquine (PQ)), photo-induced hydrolysis (e.g., sulfacetamide (SF)), and photo-induced ring cleavage (e.g., norfloxacin (NF)).

8.7.7 Effect of Temperature

High temperature results in the increased collision between drug molecules in an aqueous medium that leads to the degradation/decomposition of drugs (i.e., RF [80], meropenem (MP) [81], glibenclamide (GA) [82], etc.). The rate constant for the degradation of drug in relation to temperature is expressed by the Arrhenius equation (Eq. 8.8).

$$k = \mathrm{A}e^{\frac{-\mathrm{E}_a}{k_{\mathrm{B}}\mathrm{T}}} \tag{8.8}$$

8.7.8 Hydrolysis

The most common factor that influences drug stability is hydrolysis, especially in cases of drugs in aqueous medium or liquid formulations (i.e., aspirin (ASA) [83], RF [84], CP, florfenicol (FF), spiramycin (SM) and tylosin (TY) [85], etc.). Hydrolytic degradation of drugs is influenced by the pH of the medium.

8.7.9 Oxidation

Oxygen and oxidizing agents (i.e., H_2O_2, $KMnO_4$, etc.) leads to the oxidative degradation of drugs (i.e., AA [86], morphine (MO) [87], vitamin A [88]). When these drugs are exposed to oxygen during manufacturing or storage, their drug content is altered. The pH of the medium enhances the oxidative degradation of drugs due to the change in the redox potential of the species in the drug molecules.

8.7.10 Effect of Catalytic Agents on Drug Stability

There are different types of catalysts (i.e., organic and inorganic catalysts) which could affect the stability of drugs in different media (i.e., aqueous solution, polar and non-polar solvents). The effects of these catalysts on the stability of drugs are discussed below.

8.7.11 Inorganic Catalysts/Synthetic Catalysts

Metal ions (i.e., Cu^{2+}, Fe^{3+})- and metal chelates-catalyzed oxidation of ascorbic acid (AA) have been evaluated. The study has been carried out in the pH range of 2.0 to 5.5 where only monoionic species of AA were found to be reactive toward molecular oxygen ($^3O_2$). It has also been noticed that un-catalyzed oxidation of AA was proportional to the concentration of $^3O_2$. Furthermore, the direct oxidation of ascorbate anion (AH^-) has also been found to be influenced by $^3O_2$. The catalytic oxidation of AA caused by metal ions follows first-order kinetics depending on the concentration of $^3O_2$. In the case of Cu^{2+}-catalyzed oxidation of AA, the rate of oxidation increases with an increase in the pH from 1.5 to 3.5, whereas Fe^{3+}-catalyzed oxidation of AA increases from pH 1.50 to 3.0 and afterward decreases to pH 3.5. The difference in the catalytic activity of these metal ions (Cu^{2+}, Fe^{3+}) toward monoionic and neutral species of AA is due to the extent of the formation of metal complexes [89].

The effect of metal ions and chelating agents on the degradation of DNA by bleomycin (BM) has been carried out. In this study, the effect of reducing agents (i.e., 2-mercaptoethanol, dithiothreitol, reduced nicotinamide adenine dinucleotide phosphate, hydrogen peroxide, ascorbate) has been evaluated on the degradation of DNA by BM. It has been found that BM at a concentration of 10 μg/ml has a minimum effect on the degradation of DNA. However, at a higher concentration of BM (50 μg/ml), it decomposes DNA. In the presence of ethylenediaminetetraacetic acid (EDTA) (10^{-3} M), the degradation of DNA by BM was fully diminished. Deferoxamine is a strong and highly specific chelator of Fe^{3+} and has greater inhibition in the degradation of DNA in the presence of BM as compared to that of EDTA, whereas 2-mercaptoethanol enhanced the decomposition of DNA by BM and additionally Mg^{2+} ions along with 2-mercaptoethanol further accelerate its decomposition [90]. The effect of metal chelates (Fe^{3+}-EDTA) on the degradation

of hyaluronic acid has been carried out. It has been found that the degradation of HA was strongly inhibited by superoxide dismutase and catalase. However, in the presence of Fe^{3+} ions, degradation of HA via an autoxidation was weakly inhibited by catalase whereas unaffected in the presence of superoxide dismutase. Furthermore, penicillamine (1.0–5.0 mM) also enhanced the degradation of HA in the presence of Fe^{3+}-EDTA chelates [91].

Fosinopril (FP) is an angiotensin-converting enzyme inhibitor. Kinetics and mechanism of metal ions (i.e., Mg, Co, Mn, Zn, Ni, Cu, Fe, Ca, and Ba)-mediated degradation of FP in methanol have been determined. It has been found that these metal ions enhanced the degradation of FP. Rate constants (k) for the degradation of FP in the presence of metal ions have been determined with a decrease in the concentration of FP. The rate of degradation of FP in the presence of metal ions was in the order of $Co^{2+} > Mn^{2+} > Mg^{2+} > Zn^{2+} > Ni^{2+} > Mn^{3+} > Cu^{2+} > Fe^{2+} > Ca^{2+} > Ba^{2+}$. Electron paramagnetic resonance (EPR) spectroscopy has been used to identify the mechanism of metal ions-mediated degradation of FP and was due to the formation of FP-metal ion complex followed by deprotonation [92].

In the presence of RF (as sensitizer), Cu^{2+}-mediated degradation of calf thymus DNA and supercoiled pBR322 has been observed. It has been found that the rate of degradation of DNA was higher in the presence of Cu^{2+} and RF as compared to RF alone. The rate of reaction for the degradation of DNA has also been found to be dependent on the presence (aerobic condition) and absence (anaerobic condition) of oxygen. In anaerobic conditions, this reaction was inhibited. RF act as a reducer of Cu^{2+} which converts it into Cu^{1+} and this mechanism was confirmed by Cu^{1+} sequestering neocuproine reagent. Cu^{2+} concentration plays an important role in the degradation; therefore, with an increase in the concentration of Cu^{2+} from 5.0–25.0 μM, the percent degradation of DNA also increased from 21.5 to 40.6% [93].

Peptides methionine residues were converted into methionine sulfoxides due to the action of oxygen, metal (i.e., Fe^{3+}), and electron donors (i.e., ascorbic acid, dithiothreitol (DT)). A study has been carried out to inhibit the oxidation process at different pH in the presence of hydroxyl radical scavengers (superoxide dismutase) and azide. Superoxide dismutase has been found to possess minimum oxidative effect which indicates that superoxide radical does not have any effect on the methionine residue oxidation. In this study, the effect of Fe^{3+} combined with AA and DT on two peptides (HM and GGGMGGG) to affirm the generation of oxygen species. These two peptides were degraded in the presence of AA (2 mM)/ Fe^{3+} (0.02 mM) and DT (2.0 mM)/ Fe^{3+} (0.02 mM) and phosphate buffer (pH 7.0, 10 mM). The degradation kinetics of peptide was found to be dependent on the nature and activity of pro-oxidants. In the presence of AA/ Fe^{3+} and DTT/ Fe^{3+}, the degradation of HM follows zero-order and first-order kinetics, respectively [94]. Degradation kinetics of cefaclor (CF) (an antibiotic) in the presence of Cu^{2+} as a catalyst has been evaluated. Cu^{2+}-catalyzed hydrolysis of CF has been determined using UV-visible spectroscopy. It has been observed that Cu^{2+} slightly increased the degradation of CF in aqueous media, whereas it was markedly increased in the case of other cephalosporins. This slight increase in the rate of CF

hydrolysis was due to the interaction of Cu^{2+} with the side-chain or carboxyl group [65].

The effect of pH, Cu^{2+}, and EDTA on photolytic and oxidative degradation of antiemetic (RG12915 (RG1)) has been evaluated. It has previously been known that when RG1 is exposed to artificial fluorescent light, dichlorination and substitution occur in an aqueous medium. Transition metals are known to catalyze the autoxidation of hydrocarbons. It has been found that with the addition of Ni^{2+} and Fe^{2+} to the solution of RG1, there was no significant effect found on the auto-oxidation. However, when Cu^{2+} was added in the solution of RG1, the degradation rate was significantly increased. This increase in the rate of degradation of RG1 may be due to the initiation of an auto-oxidation reaction [95].

Zn^{2+}-based catalytic degradation of four penicillins including amoxicillin (AX), ampicillin (AP), penicillin G (PG), and V (PV) in methanol at 20 °C has been carried out. The kinetic scheme for the degradation of these drugs in the presence of Zn^{2+} has also been reported in this study. It has been found that PV degradation occurs with the formation of a single intermediate substrate–metal (SM) complex. However, other drugs degraded with the formation of the metallo complex (MC1 and MC2). This Zn^{2+}-catalyzed degradation of drugs follows first-order kinetics with the rate constants of 0.93, 2.88, 3.04, and 3.49×10^2 min^{-1} for AX, AP, PV, and PG, respectively [96].

Oxidative degradation of HA in oxidation system containing AH^-, Cu^{2+}, and H_2O_2 have been carried out in the presence and absence of drug-naproxen (NP) or acetylsalicylic acid (ASA). It has been found that the solution containing HA results in decrease viscosity, which is an indication of polymer degradation. By the addition of drug in HA solution, it has been found that the degradation of the polymer was inhibited. Fragmented/decomposed polymers were characterized using FTIR spectrometry, size exclusion chromatography (SEC), and high-performance liquid chromatography (HPLC) [97].

Spectrometric studies have been carried out to evaluate the extent of degradation kinetics of doxycycline (DX) in the presence of Cu^{2+} and H_2O_2. The degradation of DX follows pseudo-first-order kinetics. The effect of temperature, pH, Cu^{2+}, and H_2O_2 on the degradation kinetics has been determined. Reactions for the degradation have been carried out in the temperature range of 20–35 °C and there was no effect of temperature at 20–30 °C. However, at higher temperature, the reaction rate was accelerated at the initial time but afterward, it gets slower. The effect of pH (7.8–10.2) on the rate of degradation has also been carried out, and it has been found that at pH 8.6, the rate of degradation was higher whereas at pH 10.2 the rate was lower. The effect of Cu^{2+} ion and its concentration ($1.33–4.33 \times 10^{-5}$ M) on the degradation rate have also been determined. In the concentration range of $1.33–3.33 \times 10^{-5}$ M, the degradation rate follows pseudo-first-order kinetics, whereas at higher concentration, the degradation rate follows negative pseudo-first-order kinetics. However, with an increase in the concentration of Cu^{2+} rate of degradation increased. The degradation kinetics for the DX in the presence of H_2O_2 follows similar behavior as with Cu^{2+} ion. At the concentration of 1.00–2.00×

10^{-2} M, H_2O_2 follows pseudo-first-order kinetics, whereas at higher concentrations, it follows negative pseudo-first-order kinetics [98].

In the presence of ruthenium (Ru^{3+}), the catalytic oxidation of amitriptyline (AM) by potassium permanganate has been carried out at a constant ionic strength (0.20 mol/dm^3). In acidic medium, it has been found that the rate of catalytic oxidation was increased with an increase in acid concentration. The rate of catalytic oxidation was found to be eightfold higher in the presence of Ru^{3+} as compared to that of the uncatalyzed reaction. The effect of temperature on the Ru^{3+} base-catalyzed oxidation has also been determined, and it has been found that with an increase in temperature, the rate of Ru^{3+}-catalyzed oxidation of AM also increased [99].

Photodeposition technique has been used to prepare silver-doped TiO_2 (Ag-TiO_2) NPs and was characterized by scanning electron microscopy (SEM), transmission electron microscopy (TEM), X-ray diffraction (XRD), and energy dispersive X-ray (EDX) spectroscopic techniques. SEM and EDX analysis showed a dispersion of Ag metal on the surface of TiO_2. The photocatalytic property of these prepared NPs has been determined for the removal of chloramphenicol (CP) after UV irradiation. The effect of experimental parameters (i.e., doping concentration of Ag, the concentration of photocatalyst, calcination temperature) on the photocatalytic activity of on CP has been determined. It has been found that the photocatalytic activity of TiO_2 doped with Ag increases at the calcination temperature of 300 °C [100].

Analgesic drug (dipyrone (DP)) is degraded by hydrolysis to form 4-methylaminoantipyrine (4-MAA). Oxidation processes (Fenton (FP), photo-Fenton (PFP), UV/H_2O_2 photolysis (UVP), UV/TiO_2 photocatalysis (UPC)) have been carried out for the comparison of efficiency to remove 4-MAA from aqueous media. It has been found that the removal of 4-MAA through oxidation processes was 94.1, 96.4, 74.4, and 71.2% for FP, PFP, UCP, and UPVC, respectively. The removal of 4-AMM was due to the breakdown of three methyl moieties, followed by pyrazolone ring breakage leading to the formation of different intermediates. These intermediates were hydroxylated and carboxylic derivatives. The removal of 4-MAA has been carried out by varying concentrations of Fe^{2+} and H_2O_2 and pH from 1–3 mM and 5 to 25 mM and 2.0 to 4.0, respectively. The 4-MAA removal efficiency was enhanced with an increase in the concentration of Fe^{2+} and H_2O_2 and pH. The mechanism of degradation of DP is based on the formation of the oxidizing agent. However, the extent of degradation of DP and the formation of intermediates is based on the pH and concentration of Fe^{2+} and H_2O_2 [101].

TiO_2-SiO_2 composites with different concentrations of TiO_2 (10–40%, *w/w*) have been prepared using mesoporous NPs (MNPs) and characterized by N_2-physisorption, X-ray powder diffraction (XRPD), diffusive reflective UV-vis spectroscopy (DRUV-vis), X-ray photon spectroscopy (XPS), and TEM. The prepared composites were spherical with high surface area and titania was found in the anatase phase. The physical and chemical properties of these composites are specific for the catalytic process so, therefore, they were used for the photocatalytic degradation of methylene blue (MB), methyl orange (MO), and paracetamol (PM). The MNPs provide special characteristics to these composites, i.e., increase surface

area and thermal stability, and also modify their photocatalytic properties. It has also been found that loading on TiO_2, the particle size and surface characteristics influence the degree of UV absorption and energy bandgap between composites. Under UV irradiation, in the presence of TiO_2–SiO_2 composites, the concentration of MB and MO were found to decrease with the time. The photocatalytic activity of these prepare nanocomposites has been tested for the degradation of PM. It is a neutral compound that possesses a phenolic ring and has been found to adsorb on the surface of photocatalyst that results in the stabilization because of its neutral nature [102].

Photocatalytic degradation of chloramphenicol (CP) and tartrazine (TZ) has been carried out in an aqueous suspension of silver-modified TiO_2 (Ag/TiO_2) nanoparticles (NPs) after UV irradiation. These Ag/TiO_2 NPs were prepared by chemical reduction and were characterized using XRD, SEM, energy dispersive X-ray microanalysis (EDX), TEM, and XPS techniques. XPS measurements indicated that the Ag was present in the Ag^0 form on the surface of TiO_2 NPs. The effect of calcination temperature, Ag concentration, loading on photocatalyst, substrate initial concentration, and intensity of light has been evaluated on the photocatalytic degradation of CP. The results obtained after photocatalytic degradation of CP and TZ indicated with an increase in the concentration of Ag on TiO_2 NPs enhance degradation. However, the results obtained showed that the degradation of TZ (89%) was greater as compared to that of CP (84%) in these sets of experimental conditions [103]. One-pot simple synthetic method (green method) has been used to prepare doxycycline (DX)-stabilized silver nanocatalyst (DX-AgNPs) for the rapid catalytic degradation of ibuprofen (IB) and paracetamol (PM). These nanocatalysts were characterized by UV-vis spectrometry and TEM. UV-vis spectrometry of these nanocatalysts showed surface plasmon resonance (SPR) band at 404 nm. TEM analysis confirmed that the prepared nanocatalysts are spherical shaped and monodispersed with a particle size of 6.87 ± 2.2 nm. These nanocatalysts show excellent photocatalytic properties with 100% degradation of IB and PM in 1 min [104].

A photocatalytic (solar irradiation) degradation study on anti-inflammatory (ibuprofen (IB)) drug has been carried out using transition metals (Bi and Ni) doped TiO_2. Nanoparticles (NPs) of TiO_2 doped with Bi and Ni have been prepared using sol–gel method and were characterized using XRD, SEM, UV-vis reflectance spectroscopy, and Brunauer–Emmett–Teller (BET) analysis. These catalysts (metal-doped NPs) were synthesized by different concentrations (0.25–1.0, *w*/*w*) of the doped materials. IB was used as a model compound to evaluate the photocatalytic property of these doped NPs and compared with the Degussa TiO_2 to evaluate the kinetics of the drug degradation. Bi-doped TiO_2 NPs showed higher photocatalytic degradation of IB as compared to that of Ni-doped TiO_2 NPs or Degussa NPs. IB decomposition was found to be 89 and 78% after irradiation with Bi-doped TiO_2 and Ni-doped TiO_2 NPs, respectively. Kinetics of degradation of IB in these experimental conditions has been determined using the Langmuir–Hinshelwood model and found that its degradation follows first-order kinetics with

the degradation rate (k) of 6.40 and 4.60 $\times$ 10^{-3} min^{-1} for Bi and Ni-doped TiO_2 NPs-mediated photocatalysis, respectively [105].

Photocatalytic activity of semiconductors could be increased by doping them with rare earth metals nanoparticles (NPs). The gel combustion method has been used to prepare zinc oxide (ZnO) and lanthanum (La)-doped ZnO NPs. It has been found that when La is used as doping material of ZnO NPs, the cytotoxicity and photocatalytic activity were enhanced toward difference cell lines and paracetamol (PM) drug. These prepared doped ZnO NPs were characterized by UV-vis spectroscopy, SEM, TEM, XRD, and FTIR spectrometry. The spectroscopic studies showed that La-doped ZnO NPs exhibited absorption maxima in the visible region due to the presence of La [106].

Bimetallic (Fe and Ni) NPs have been synthesized and were characterized by SEM, energy-EDS, and XRD analysis. These bimetallic NPs were found to be in the particle size range of 20–200 nm and were used to determine their reductive degradation effect on nimesulide (NM). SEM confirmed that the prepared NPs are uniformly bound with silica and XRD analysis showed the presence of Ni and Fe on silica. Reductive degradation effect on NM was evaluated using bimetallic NPs containing Ni (8%, *w/w*) at an agitation frequency of 250 rpm. The reductive degradation products after degradation were determined using liquid chromatography-coupled electron spray ionization mass spectrometry (LC-ESI-MS). This study has confirmed that the degradation of NM mainly occurs through the reduction of the nitro group and the elimination of sulphonyl moiety. This reductive degradation of NM leads to the formation of an amine and thioester aromatic as byproducts [107].

The sol–gel method has been used to prepare carbon-doped WO_3/TiO_2 photocatalysts. These prepared photocatalysts were characterized using XRD, diffuse reflectance UV-vis spectroscopy, nitrogen adsorption-desorption analysis, SEM, TEM, and XPS. The photocatalytic activity of these modified mixed oxides has been evaluated for the degradation of sodium diclofenac (SDF) by solar irradiation. High-performance liquid chromatography (HPLC), total organic carbon (TOC) analysis, and ion chromatography (IC) have been used to evaluate the degradation and mineralization of SDF. Tungsten and carbon (TWC)-modified photocatalyst exhibits higher activity as compared to that of TiO_2 and WO_3/TiO_2 for the degradation SDF [108].

A mechanistic study and degradation pathway for the photocatalytic degradation of fluoroquinolone (levofloxacin (LF)) using quantum dots (QDs) (Ag_2O/TiO_2) has been carried out. The QDs were prepared using a pH-mediated precipitation method and were characterized for their morphology, composition, structure, optical, and photocatalytic properties. Morphological studies confirmed the formation of QDs with a particle size of 2–9 nm. XPS analysis for surface indicates that the Ag^+ and Ti^{+4} were present in the form of Ag_2O and TiO_2 on the surface of QDs. Spectroscopic properties reveal that the absorption maxima of Ag/TiO_2 QDs shift to the longer wavelength (506 nm) as compared to TiO_2 QDs (394 nm). It has been found that these QDs possess excellent photocatalytic properties for the degradation of LF as compared to that of TiO_2 QDs. This excellent photocatalytic property was

attributed to the electron-hole pair separation that results in the higher absorption of light [109].

The study has been carried out to evaluate the metal ion (Fe^{3+})-catalyzed oxidative degradation of some aromatic drugs i.e., dextromethorphan (DM), epinastine (EP), brodimoprim (BD)/drug fragment that possesses C-H bonds in the absence of peroxides. Fe^{3+} is known to oxidize peroxides to form peroxy and alkoxy radicals which oxidize drug molecules. Transition metals are known to oxidize electron-rich centers of aromatic rings which results in the formation of aromatic radical cations. This aromatic radical cation, when attached to the benzylic side-chain, will overlap the σ-orbital with the hydrogen of the benzylic ring system and leads to the breakdown of the C-H bond. H atom from the C-H bond is then transferred to the aromatic ring, which leads to the formation of benzylic radical. This benzylic radical in an oxygen-saturated system react with oxygen to form peroxy radical. This peroxy radical follow the Russell mechanism, which results in the formation of alcoholic and ketonic degradation products [110].

Spectroscopic and thermal degradation of Mg^{2+}, Ca^{2+}, Ba^{2+}, and Sr^{2+} of PM has been carried out. Complexes of Mg^{2+}, Ca^{2+}, Ba^{2+}, and Sr^{2+} of PM have been prepared and characterized by elemental analysis, thermogravimetric analysis (TGA), conductivity, UV-vis spectrometry, IR, and ^{1}H NMR spectroscopy. Molar conductivity values for these metal complexes were found to be in the range of 57.4 to 72.8 $cm^2\ mol^{-1}$. The microanalytical analysis revealed that there was a 2:1 molar ratio complex between PM and metal ions [111]. The microwave hydrothermal process has been used to prepare Ag-dispersed $BaMoO_4$ octahedron microcrystals doped with Er^{3+}, Yb^{3+}, and K^+. These doped microcrystals were characterized by XRD, XPS, UV-vis diffuse reflectance spectrometer, Raman spectroscopy, and field emission scanning electron microscope (FESEM). The photocatalytic activity of these prepared microcrystals for the degradation of rhodamine B (Rh B) and IB after solar and visible irradiation, respectively, has been determined. In the presence of these doped (Er^{3+}/Yb^{3+}) microcrystals, the degradation of Rh B and IB was around 99.60 and 41.50% in 90 min, respectively. Degradation products after irradiation of IB in the presence of doped microcrystals have been identified by high-resolution quadruple-time of flight-electrospray ionization mass spectrometry (HR-QTOF ESI/MS) in negative ion mode [112].

The effect of metal ions (monovalent, divalent, and trivalent) on the degradation of riboflavin (RF) has been evaluated in aqueous media. This study has been carried out in low (0.2 M) and high (0.4 M) phosphate buffer concentration at pH 7.0. These metal ions include Ag^+, Zn^{2+}, Mg^{2+}, Pb^{2+}, Mn^{2+}, Cu^{2+}, Cd^{2+}, Fe^{2+}, Ca^{2+}, Co^{2+}, Ni^{2+}, and Fe^{3+}. RF (5.0×10^{-5} M) was photolyzed at pH 7.0 with these metal ions ($1.0–5.0 \times 10^{-4}$ M), and it was found that with an increase in the concentration of metal ions, the rate of photolysis also increases. It has been found that except Ag + ions, all other metal ions accelerate the degradation of RF. The second-order rate constants for the interaction of these metal ions with RF are in the order of $Zn^{2+} > Mg^{2+} > Pb^{2+} > Mn^{2+} > Cu^{2+} > Cd^{2+} > Fe^{2+} > Ca^{2+} > Fe^{3+} > Co^{2+} > Ni^{2+} > Ag^+$. These metal ions form a metal-RF complex in the ground state which on irradiation forms exciplex due to charge transfer which leads to the formation of

semiquinone radical and oxidized metal ion. This semiquinone radical combine with another semiquinone radical to form reduced RF which was then oxidized to give degradation products [113].

ZnO NPs for nanocatalysis has been prepared for the catalytic degradation of amlodipine besylate (AMB). These prepared NPs were characterized using SEM, XRD, FTIR, BET, Barrett-Joyner-Halenda (BJH), EDS, X-ray fluorescence (XRF), and UV-vis spectrometry. Different degradation parameters (i.e., initial concentration, nanocatalyst concentration, pH, temperature, time of visible irradiation, H_2O_2) were used to evaluate the parameters dependent on degradation of AMB. The initial concentration of analyte plays an important role in the rate of degradation; therefore, it has been found that at higher concentrations of AMB, the catalytic efficiency of these NPs was reduced due to the absorption of AMB on the surface of these NPs. The photocatalytic activity of ZnO NPs was found to be maximum at 3 mg whereas at higher concentrations of nanocatalysts, the photocatalytic activity would not be observed. Previously it has been reported that AMB degraded more rapidly in the alkaline region as compared to that of the acidic region. However, these nanocatalyst dissolved in a highly acidic medium, so for this reason, Fe^{2+}-doped ZnO NPs are the best catalyst for the degradation of AMB at all pH range. The rate of reaction was temperature dependent, and at a higher temperature (80 °C), nanocatalyst accelerates the degradation of AMB [114].

8.7.12 Organic Catalysts/Natural Catalysts

Chondroitin sulfate (CS) is a naturally occurring polymer containing glucuronic acid and N-acetyl glucosamine. CS is sulfated at one position (either 4 or 6) and is used for the treatment of osteoarthritis. The stability of CS has been determined in the presence of tissues and lumenal components of the stomach, small intestine, cecum, and colon. It has been found that the components of tissues, stomach, and small intestine do not degrade CS, whereas the components of cecum and colon promoted its degradation. ^{14}C-radiolabelled CS has been used to determine the degradation of CS and its degradation products (disaccharides). In vitro degradation of CS has been carried out in the presence of commercially available chondroitinase which is determined using the spectrometric method. This method has confirmed that in the presence of chondroitinase, the degradation of CS has been around 80%, whereas in the presence of stomach and intestinal components, no degradation has been found. In vitro transport mechanism of CS across the gastrointestinal tract has also been determined using ^{14}C-radiolabelled CS and found that CS transportation across the small intestine was via endocytosis [115].

Glutathione S-transferase (GSTs) enzymes have been used to evaluate the degradation of some antibiotics including tetracycline (TC), sulfathiazole (SF), and ampicillin (AM). GSTs are the proteins that catalyze the conjugated system of reduced glutathione in the presence of hydrophobic substances having electrophilic centers. In the presence of GSTs, these antibiotics are converted into non-toxic

byproducts in the range of 30 to 70%. The conversion of these antibiotics in byproducts was 30% for TC and 60–70% for SF and AM [116].

Catalytic degradation of amygdalin (AMD) with enzyme from *Aspergillus niger* has been carried out. AMD was a controversial drug that has been used as an anti-cancerous agent for many years. It has previously been found that AMD itself does not possess any anti-tumor activity, but its degradation products might possess anti-cancerous activity. AMD was exposed to the extracellular enzyme from *Aspergillus niger* for catalytic degradation at 37 °C and found that in 4 h, it was degraded into four degradation products. These four degradation products are then isolated and purified using chromatography and further characterized by mass spectrometry, ^{13}C, and ^{1}H NMR. These products have been identified as mandelonitrile, prunasin, phenyl-(3,4,5-trihydroxy-6-methyl-tetrathydro-pyran-2-yloxyl)-acetonitrile (PTMT) (a novel hydroxy derivative of prunasin), and benzaldehyde. This novel hydroxyl derivative (PTMT) has been found to inhibit the growth of S-18 tumor cells in 11 days, depending on the concentration of PTMT [117].

A study has been carried out on the effect of enzymes isolated from *Planococcus* sp. S5 (gram-positive bacteria) on the degradation of naproxen (non-steroidal inflammatory drug (NSAID)) (NX). It has been found that in the presence of these enzymes, the degradation was around 27%. The influence of growth substrates (i.e., benzoate, 4-hydroxybenzoic acid, 3,4-dihydroxybenzoic acid, vanillic acid) on the degradation of NX has also been evaluated. It has been found that the degradation of NX was around 21.5, 71.7, 14.7, and 8.2% in the presence of benzoate, 4-hydroxybenzoic acid, 3,4-dihydroxybenzoic acid, and vanillic acid, respectively. Furthermore, it was noticed that *Planococcus* sp. S5 possesses an excellent ability for the degradation of NX in the presence of 4-hydroxybenzoate (carbon source) [118].

White-rot fungus *Pleurotus djamor* has been used to evaluate the degradation kinetics of NSAIDs (i.e., NX, diclofenac (DF), ketoprofen (KP)) in pure, mixtures, and submerged cultures. It has been found that DF alone and in the mixture (NX and KP) the removal was around 93 and 99%, respectively, in the presence of fungus after 6 h of incubation. After 48 h of incubation with fungus, the removal of NX and KP was around 90 and 87%, respectively. The catalytic activities of enzyme laccases, manganese, peroxidases, and lignin peroxidases on the degradation kinetics of NSAIDs have also been carried out. The catalytic activity of extracellular laccases increases in the range of 200–300% for the degradation of NSAIDs in submerged cultures. However, in the case of manganese peroxides, the activity was increased to 126 and 138% for DF and other NSAIDs, respectively. The catalytic activity of lignin peroxides for the degradation of NSAIDs in the mixture was around 23% [119].

8.8 Conclusion

Catalytic agents are specific for different chemical/biological reactions, and their use in different processes is an important attribute to enhance the processes rather than to destroy the final product or the formation of unwanted products. Catalytic reactions

are useful as they lead to the formation of different products which sometimes may be beneficial for the treatment of different diseases. However, these reactions may also sometimes cause toxic effects on the biological system and alter normal physiological functions.

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