Catalase enzyme activity pdf

Jet species produced in a cell during normal cellular metabolism can chemically react with cellular biomolecules such as nucleic acids, proteins and lipids, causing oxidative changes leading to changes in their composition and potential damage to their cellular activity. Fortunately, the cells have developed several antioxidant defense mechanisms (like metabolites, vitamins and enzymes) to neutralize or mitigate the harmful effects of reactive species and/or their by-products. Any disturbance of the balance in the level of antioxidants and reactive species leads to a physiological condition called oxidative stress. Catalase is one of the most important antioxidant enzymes that mitigates oxidative stress largely by destroying hydrogen cellular peroxide to produce water and oxygen. Deficiency or malfunction of catalase is postulated to be associated with the pathogenesis of many age-related degenerative diseases such as diabetes, hypertension, anemia, vitiligo, Alzheimer's disease, Parkinson's disease, bipolar disorder, cancer and schizophrenia. Therefore, many laboratories are working to study its use as a potential drug for the treatment of such diseases. This paper describes the direct and indirect involvement of deficiency and/or modification of catalase in the pathogenesis of certain important diseases such as diabetes, Alzheimer's disease, Parkinson's disease, vitiligo and acatalazemia. Details of efforts to study the potential treatment of these diseases using catalase as a protein therapeutic agent have also been described.1 IntroductionReactive Species (RS) are highly active moieties, some of which are direct oxidizers, and some are oxygen or oxygen-like electronlegative elements produced in the cell during cellular metabolism or in pathological conditions. Some of the jet species are free radicals such as hydroxyl radical and superoxide radicals, and some are negligent, such as hydrogen peroxide. Free radicals are any independent species consisting of one or more unsparable electrons in their atomic or molecular orbit. They are usually unstable, short-lived, but usually chemically reactive. They can react with any molecule either by oxidizing it or by causing any other kind of chemical modification. Free radicals can potentially oxidize all cellular biomolecules, including nucleic acids, proteins and lipids. For example, peroxide oxidation of omega-6 polyunsaturated fatty acids (such as arachidonic acid and linoly acid) leads to the production of 4-hydroxynonal (HNE), which is one of the main reactive aldehydes produced by oxidative stress. There are many jet species and free radicals that are listed in Table 1.Reactive Oxygen Species (ROS)Superoxide (O2·-), Hydroxyl Radical (OH·), Hydrogen Peroxide (H2O2), Alcoxil Radical (RO·), lipid alcoxyl (LO·), Peroxil radical (RO2), ozone (RO·), ozone (O3), ozone ozone (LOOH), singlet oxygen (1O2), hydropecoxic radical (HO2·)Reactive types of chlorine (RCS)Hypochloritis ion (OCl), nitrilchloride (NO2)Reactive nitrogen species (RNS)Nitrogen oxide (NO·), nitric acid (HNO2), nitrosonic (NO), nitrosonic acid (NO) (NO-), peroxynitrit (ONOO-), nitrogen dioxide (NO2), alkyl-pecoxinitrite (ROONO) Reactive sulfur species (RSS)Thiyl radical (R-S·), pertile-radical (RSS·)These free radicals are formed in the cell with normal cellular metabolism as a mitochondrial electronic transport chain , β fatty acid oxidation, and cytochrome P450-mediated reaction and respiratory explosions during immune defenses. For example, autooxidation of certain biologically important substances, such as FADH2 and tetrahydroperidine, can bring O2·-in the presence of oxygen. The imbalance between the production and the swollen of these reactive substances through antioxidant mechanisms causes oxidative stress. The loss of functionality and adaptability of important biomolecules due to oxidative stress are two interdependent biological processes that are among the important factors that mediate aging. The free radical hypothesis, also known as the oxidative stress hypothesis, is one of the strongly supported theories that can determine the causes of the aging process. Oxidative stress has been involved in many metabolic and neurological degenerative disorders. Degenerative diseases, where the function and structure of tissue or organs deteriorate over time, such as Alzheimer's disease, Parkinson's disease, diabetes, cataracts, cancer and cardiovascular disease, have been attributed to oxidative stressors and the natural aging process. Thus, oxidative stress, aging and degenerative diseases are interconnected. The body has a defense mechanism against oxidative stress, in which both ensimatic and non-rinmatic molecules are the two main components. This antioxidant protection system consists of some enzymes, some proteins and several low molecular mass molecules. Antioxidant enzymes can catalytically remove reactive species. For example, superoxide dismutase dismutase dismutates superoxide in hydrogen peroxide, which in turn degrades as a result of catalase or glutathione peroxidase. The relationship between different antioxidant enzymes is graphically depicted in Figure 1. Transferrin, metalloniaine and keruloplasmin are among the proteins that can reduce the availability of prooxidants such as the transition of metal ions like iron ions and copper ions, which can produce hydroxyl radical from Fenton's hydrogen peroxide reaction. Low molecular weight antioxidants include ascorbic acid, α tocopherol, glutathione and uric acid, which neutralize RS by cleaning the entire molecule or its by-products, by reducing it or participating in any form of chemical reaction leading to or the partial destruction of his or his by-products. The interaction of catalase with other antioxidants and proteins can be (Search tool for finding interacting genes/proteins) analysis no.4, 5. STRING is a biological database used to study the interaction of protein protein. The network analysis of catalase interactions with other STRING proteins was divided into two different modules (Figure 2). Module 1 contains four proteins that are mainly involved in peroxisom pathways, including PPC and three protein modules 2, such as SOD1 (superoxide dismutase 1), SOD2 (superoxide dismutase 2) and PRDX5 (peroxyredoxine 5) (Additional Figure 1). In module 1 ACOX1 (peroxysomal akyal coenzyme oxidase), HSD17B4 (peroxysoma multifunctional enzyme) and HAO1 (hydroxicide oxidase 1) are involved in the oxidation pathway of fatty acids in peroxysomes, While the daO protein (D amino acid oxide) is involved in the metabolism pathway of amino acids in peroxysomema (. All components of module 1 are involved in various metabolic pathways. Proteins in module 2 are mainly involved in responses to oxidative stress. AKT1 is a serin-trionin protein called kinase that is involved in cell survival, metabolism, growth, and angiogenesis. All proteins of both modules 1 and 2, including CPR, have catalytic activity and are located in the lumen of intracellular organelles. SOD2 and AKT1 modules 2, including CAT, were involved in the pathway of regulating longevity and the signaling pathway of FOXO in mammals (Additional figures 2 and 3). But in many other species, SOD1 and SOD3 (superoxide dismutase 3) were also involved along with SOD2, AKT1, and PPC (Additional Figure 4). Among reactive types of hydrogen peroxide is free diffusion and relatively long-term. It acts as a weak oxidation as well as a decrease in the agent; However, it is not very reactive, but it is the progenitor of many other reactive oxygen types (ROS). It has been demonstrated to oxidize glyceraldehyde-3-phosphate dehydrogenase by oxidizing the sexual main groups of thyol in the active location of this enzyme. In most cellular injuries, this molecule is known to play an indirect role. One of the most important products is the formation of a more reactive free radical ·OH sweeping in the presence of the transition of metal ions such as Fe2 using the Fenton reaction. There are many enzymes that are able to neutralize hydrogen peroxide. These enzymes include catalase, glutathyone peroxidase and other peroxidase such as cytochrome to peroxidase and peroxidase NADH. Catalase is a key enzyme that uses hydrogen peroxide, a non-radical ROS, as a substrate. This enzyme is responsible for neutralizing hydrogen peroxide by decomposing, thereby maintaining the optimal level of the molecule in the cell, which is also important for cellular signaling processes. The importance of the enzyme can be assessed by its fact and indirect involvement in many diseases and infections. This review attempted to correlate the role of catalysis with pathogenesis and the progression of stress-related oxidative diseases. A brief account of catalysis, its isoforms, structure and reaction mechanism, as well as its association with some common important disorders, is described in this review article.2 CatalaseA catalysis (E.C. 1.11.1.6) is one of the most important antioxidant enzymes. It is present in almost all aerobic organisms. Catalase breaks down two hydrogen peroxide molecules into one oxygen molecule and two water molecules in a two-step reaction. The same is presented in Figure 3, obtained from Ivancic et al. The first step of the reaction mechanism involves the formation of spectroscopically different intermediate compounds I (Figure 3(a) which is a covalent species of oxyferril (FeIVO) having porphyrin π-cation radical, by reducing one molecule of hydrogen peroxide. In the second stage of the reaction (Figure 3(b),, the compound I is reduced through the reactions of the redox by two electrons of transmission from the electron donor (the second molecule of hydrogen peroxide) to produce a free enzyme, oxygen and water. (a) (b) (b) (b) In 1937, the protein was first crystallized from the bovine liver in the Sumner and Downs laboratory. The first prokaryotic catalysis was cleared of the aerobic bacterium Micrococcus lysodeikticus in 1948. Gene coding for catalase is the CAT gene that is located in chromosome 11 in humans. In the following decades, several studies of prokaryotic catalase were conducted, as well as the lower eukaryotic catalase. In particular, catalase studies from Saccharomyces cerevisiae have generated data and information about the evolution of the enzyme at the molecular level. It has also been reported that catalase is an important enzyme implicated in mutagenes and inflammatory diseases, as well as during the suppression of apoptosis, which are known to be associated with oxidative stress conditions. Catalase is characterized by many eukaryotic as well as prokaryotic organisms. Table 2 summarizes some of the basic physiochemical information available today in the literature on catalysis of various organisms. Based on differences in their sequence and structure, there are three different types of catalase. Monofunctional hem-containing enzymes are the most common. It is present in all aerobic organisms. Two-function catalysis-peroxidase belongs to the second class, which is relatively less abundant in nature. This enzyme also contains a group of hemen. This is closely related to plant peroxidases with structural and consistency similarities. The third class belongs to the group Mn-containing catalase, which lacks the value of heme group.Organisms/organ/organelleSpecific activity (mmol/min/mg) Optimal temperature (KK)/pHInhibitors value (mM)Turnover numberMol. сапиенс эритроциты (цитоплазма), почки и печень (митохондрии, пероксисомы)27380037-C/6.8-7.53-Amino-1-H-1,2,4-triazole80---159, 160-Бос Телец liver9180025-C-35'C/6-7.53-Amino-1-H-1,2,4-triazole28.6---161-163-Oryza перекись sativa-25'C/6-10Hydrogen (выше 60 мМ)10080000234000,164, 165Vigna mungo рассада2570040 градусов по Цельсию/7Cu2, Fe2, ЭДТА, NaN316.2- 166-Escherichia coli2070022-C/6-82-Меркаптоэтанол6416300337000 Saccharomyces cerevisiae116100-NaCN (35 мМ), гидроксиламин125- »159»Люди обладают типичным монофункциональным гемесодержащей каталазой с протезной группой феррикического протопорфирина IX, который реагирует с перекисью водорода. Located in peroxysomes, the enzyme has a molecular mass of about 220-240 kDa. It is a tetramer protein with each subdivision divided into four regions, N-terminal threaded hand, C-terminal gels, wrapping loop and β barrel (figure 4). Each unit has a hydrophobic core consisting of eight β in barrels, α and heliks. These β barrels are anti-parallels with each other. The dual side of the unit consists of the first four strands of the β (No1-No4) of the domain β barrel, and the remaining four strands (No5-No8) play a role in the NADPH binding pocket. The N-terminal carving arm of the unit (remnants 5-70) intricately connects the two units, hooking through a long packing cycle (remains 380-438). Finally, the helical domain on one β barrel consists of four C-terminal helikates. Tetramerization forces the N-terminal threading arms by hand exchanged dimer to cover the heme active site for another pair of dimers and suggests that catalysis corresponds to a more general model of domain replacement with arm-sharing time later, tetramer-dependent development. Throughout the protein, water fills in the packaging defects between the four areas of the unit and between the units in the tetramer. Only hydrophobic β of the trunk and the immediate vicinity of the active area are significantly deprived of these structural water molecules. XRD studies have found that the root average square deviation (r.m.s.d.) coordinates the differences between the four units at 0.156 euros for spinal atoms, 0.400 euros for side chains and 0.125 euros for gem groups. The 3D structure of the enzyme at 1.5 was clarified in 2001. The crystalline structures of the human catalase show that the active place of the iron is pentacoordined. Negatively charged carboxilate carboxilate is a radical form of salt bridges to three residues of arginine (Arg72, Arg117, and Arg365), which are likely to aid in the burial of heme and help increase the potential of redox compound I porphyrin radical and persists in bacterial, fungal, plant and animal catalase. In addition to the hem group, the active conformation of the enzyme consists of one tightly knit NADPH molecule in each unit. There are various reports on the role of this NADPH molecule. It was demonstrated to prevent the formation of Fe (IV)oxo-ligated inactive form of catalase - hydrogen peroxide, and slowly induce the removal of inactive catalase (19, 23). Catalase deficiency or malfunction is associated with many diseases such as diabetes mellitus, vitiligo, cardiovascular disease, Wilson's disease, hypertension, anemia, some dermatological disorders, Alzheimer's disease, bipolar disorder and schizophrenia (Figure 5). It has been reported that the anomaly of catalase activity is inherited in acatalazemia, which is a rare genetic disease (also known as Takahara disease). It is an autosomal recessive trait and is characterized by a decrease in catalase levels. Catalase plays a major role in regulating the cellular level of hydrogen peroxide (28, 29), and its hydrogen peroxide catabolism protects cells from oxidative attack, for example by providing pancreatic cells β from hydrogen peroxide trauma (30, 31). Low types of catalase have been reported in patients with schizophrenia, such as also in patients with atherosclerosis. Genetic variations of the catalase gene also play a role in the pathogenesis of various diseases, which is depicted in Figure 6. Several studies have investigated the polymorphism of CAT and its participation in the development of various diseases as well as its role as a regulator in the expression of the CAT gene. Single nucleotide polymorphisms of the CAT gene in the region of protetivism may affect transcription frequencies, leading to low CPR expression (33, 34). The most common polymorphisms that affect the transcription of the CAT gene, as well as those that affect catalase activity, are -262C/T and -844G/A or -844C/T in the promoter area. There are many other polymorphisms involved in the development of numerous diseases that vary among the population. CAT -262C/T polymorphism is associated with type 1 diabetes and breast cancer. Two single-adread polymorphisms of the CAT gene, viz., 1167T/C and -262C/T are reported to have a strong association with type 1 diabetes. The functional consequence of this polymorphic position 1167T/C in exon 9 is not known. But in the case of -262C/T, the change shows significant functional significance. It affects the binding of AP-2 and Sp-1 (nuclear transcription factors), as well as affects expression, as well as the level of catalase in red blood cells. In Swedish populations, the concentration of red blood cells catalase in people carrying the TT genotype was high compared to the CC genotype. On the other hand, in Russian populations, persons carrying the CC genotype have a higher risk of developing type 1 diabetes than those carrying the TT genotype. Blood catalase levels were found to be low in CC individuals which result in stress oxidative conditions, thus promoting type 1 diabetes. Another single-veeder polymorphism of the CAT 111C/T gene in exone 9 was studied among various forms of diabetes and showed very Association .40. CAT -262C/T polymorphism has a link to breast cancer. The CC genotype showed a higher activity of catalase in red blood cells compared to TT and TC genotypes with a correlated reduced risk of breast cancer by 17%. However, it should be noted here that this population survey was conducted with a much smaller number of people. Studies have shown that the level of polymorphism -262C/T affects not only transcription activity, but also the level of catalase in red blood cells. Another common PPC polymorphism is -844C/T or -844G/A, which can lead to lower catalase levels affecting transcription frequency. CAT -844C/T polymorphism has a strong association with hypertension in the Chinese population. Hypertension is a multi-factor complex lifestyle disorder. Among Japanese populations, this -844C/T polymorphism is reported to show a strong association with hypertension. But the functional relationship is not very clear. CAT -844G/A, -89A/T and -20T/C polymorphisms have been shown to be associated with malnutrition. This polymorphism can affect the rate of transcription, thereby reducing catalase levels. -89A/T polymorphism is also reported to show a link to vitiligo and osteonecrosis (44, 45). The CAT variant -89A/T is reportedly associated with a significantly reduced level of catalase with a correlation with developing vitiligo in the Chinese population. The CAT 389C/T genotype has no association with vitiligo among the Chinese population, but the link has been established in North America and the United Kingdom (44, 46, 47). The relationship of these genotypes with the pathogenesis of vitiligo is discussed in a later section. CAT -89A/T, -20T/C, No3033C/T, No14539A/T, No22348C/T and polymorphisms 24413T/C may be involved in osteonecrosis in Korean populations. Data from all studies show different polymorphisms of the PPC gene among different populations in different regions of the world. Further demographic research is needed around the world to get a clear understanding of the link between the PPC gene and various diseases. In the future, this may open up new therapeutic approaches by regulating the CAT.3.1 gene. Diabetes MellitusDiabetes mellitus is a common disease nowadays. They are caused by a bundle of metabolic disorders that have high blood glucose levels due to improper insulin secretion or its activity or both. This can lead to other secondary ailments such as nerve damage, blindness, heart disease, stroke and kidney disease. The number of people affected by diabetes has increased significantly in recent years. Worldwide, the number of adults affected by diabetes is expected to more than double from the 135 million affected in 1995 to about 300 million by 2025 and 629 million by 2045, and much of the increase will be countries such as India. Data for 2018 from the World Health Organization (WHO) (WHO) diabetes country profile are shown in Figure 7, which shows the prevalence of diabetes among both sexes in different countries classified according to their economic status in a United Nations report. The disease appears to be more prevalent in developed countries, and the percentage of the affected population appears to be more or less unified in all of these countries. Many of the discrepancies are observed among the developing countries with the highest percentage of the population affected in Egypt. Less prevalence is observed among the least developing countries, indicating that lifestyle and nutrition play an important role in the development of the disease, as is the case in developed countries. In addition, gender appears to play a role, with women more likely to have the prevalence of the disease than men in developing countries, suggesting that social norms may also play a role. In contrast, men seem more susceptible in developed countries, indicating a possible genetic and lifestyle role in the development of the disease. There are two common forms of diabetes, type 1 and type 2. Type 1 diabetes is a juvenile form and insulin-dependent diabetes, accounting for about 10% of all cases, but it can also develop in adults. In this case, the cells β the pancreas are destroyed by autoantitorods, which makes the cells incapable of producing insulin. This autoimmune disease has a correlation between immunological and genetic factors. There are three main types of autoantial found in type 1 diabetes, such as GDP65, IA2 and insulin autoantibodies, but insulin-free antibodies can be detected mainly in young patients and may be lacking in adults. These antibodies are mainly associated with conformacial epitopes on the insulin chain B. The genetic feature shows a link between type 1 diabetes and some alleles of the HLA complex. There is a strong link between the progression of type 1 diabetes and the presence of HLA II alleles. type 2 diabetes is the most common form of the disease, accounting for approximately 90% of all diabetes cases. This is primarily due to low insulin production, and secondly, also due to insulin resistance by the body's cells. The β islets of Langerkhanov are damaged, which make them incapable of producing insulin. Oxidative stress has been demonstrated as an important factor responsible for the development of type 2 diabetes. Hydrogen peroxide has been shown to act as an oxidizer and damage the cell β, interrupting the signaling pathway of insulin production .30, 54, 55. According to a study conducted by Professor Kassab's laboratory, a four-fold increase in hydrogen peroxide was observed in type 2 diabetes patients than in healthy controls. This observation was confirmed by observations of low catalase catalase in β cells in hyperglycomial models of mice. Another form of diabetes, known as pancreatic diabetes, has been classified as type 3c diabetes (T3cDM). T3cDM is the result of pancreatitis (both acute and chronic), cystic fibrosis in pancreatic tissue, inflammation and damage to pancreatic tissue (58, 59). Damage to the exocrine peptide of the pancreas (PP) and pancreatic enzymes occurs in the early stages of pancreatic diabetes. The decrease in glycogen levels due to α damage occurs in the late stages of pancreatic diabetes. As a result, elevated levels of glucagon can lead to hyperglycemia in diabetes. There are many aspects associated with the pathophysiology of pancreatic diabetes. Immunopathogenesis is one of the important aspects that contribute to the development of pancreatic diabetes. Various pro-inflammatory cytokines such as tumor necrosis factor α, interferon γ, and interleukin 1 are involved in the pathogenesis of pancreatic diabetes. Higher concentration of cytokines leads to dysfunction β cells in the early stages of chronic pancreatitis. At higher concentrations, interleukin 1 induces apoptosis β cells by NFB. Higher concentration of interferon γ reduces transcription of the pancreas and duodenal cell 1 (PDX1), a transcription factor. PDX1 is essential for the development of pancreatic cells through the maturation of β cells, as well as through duodenal differentiation. Reducing survivability and cell differentiation β in patients with chronic pancreatitis due to loss of PDX1. Hydrogen peroxide plays a central role in this pathway as a signaling molecule. At a lower concentration, hydrogen peroxide plays as a signaling molecule, while it becomes toxic at higher concentrations, and catalysis plays an important role in maintaining cell homeostasis by degrading hydrogen peroxide. The activity of catalase in serum has been observed high in acute pancreatitis and persists at an elevated level for 10-14 days. Thus, high catalase activity can contribute to the pathogenesis of T3cDM indirectly, supporting the concentration of hydrogen peroxide, which will cause the synthesis of pro-inflammatory cytokines as a result of pancreatic diabetes. Gestational diabetes (GDM) is another common form of diabetes among pregnant women. The pathogenesis of GDM is very similar to type 2 diabetes. There are several factors, including ethnicity, maternal age, hypertension, obesity and polycystic ovary syndrome (PCOS), which are associated with the possibility of developing GDM (67, 68). Pregnant women with GDM have a higher risk of developing type 2 diabetes after pregnancy. Descendants of gestational diabetic mothers are prone to developing various diseases such as hypertension, various metabolic syndromes and chronic .69, 70. These birth defects can be due to higher concentrations of reactive oxygen and reduced antioxidant protection, which in turn make the cell more susceptible to oxidative slurs. GDM usually develops in the second and third trimesters of pregnancy. Reports of catalase's relationship with GDM are highly contradictory. Oxidative stress was reported to be high in the second and third trimesters of pregnancy, while catalase activity was also low during this period (72, 73). Blood catalase activity was reported to be low in pregnant women with GDM compared to non-violent and pregnant nondiabetic healthy control women (72). However, blood catalase activity was observed to increase in the third trimester than in the second trimester in pregnant people with GDM. In another study, low blood catalase activity was observed in pregnant women with GDM. As mentioned, there is a bad link between 111C/T polymorphism and various forms of diabetes that include GDM. Expression of mRNA of the PPC gene in the placenta of pregnant women with gestational diabetes was higher compared to expressing in normal pregnant women. Thus, it can be concluded from the above that catalasis may be related to GDM pathophysiology during pregnancy, but further research is needed to establish the facts. Hydrogen peroxide was involved as a cellular messenger in the signaling pathway for insulin secretion by inactivating tyrosinfosphatase (65, 75-78). It has been postulated that catalase in the liver can provide cellular protection by degrading hydrogen peroxide to water and oxygen. The absence of catalase can contribute to the development of diabetes (76, 79) with a positive correlation observed between diabetes in patients with akalysane. It is estimated that approximately 12.7% of patients with acatalazem/hypocathesomic diseases also suffer from diabetes. It has been suggested that catalase deficiency may be the cause of diabetes indirectly. It is known β that oxidized cells are sensitive. These cells are not only devoid of catalase, but also have a higher concentration of mitochondria, which is one of the main sources of superoxide and hydrogen peroxide in the cell through the electronic transport pathway. Thus, in acatalazemic/hypocathesic patients, a small amount of oxidative stress over a long period of time can lead to the accumulation of oxidative damage in the cells β, leading to the onset of diabetes (76, 79). There are many vascular complications in diabetes, including microvascular complications (diabetic retinopathy, nephropathy, neuropathy, etc.) and cardiovascular complications. Oxidation plays an important role in the various complications that occur in both type 1 and type II diabetes. Due to low levels of expression or catalase activity, hydrogen concentration can increase in cells creating oxidative stress conditions that cause the progression of different types of complications. In the case of retinopathy of diabetes, the retina is damaged by neovascularization of the retina, where the new origin of vessels from existing veins extends to the internal cells of the retina, leading to blindness. Vascular endothelial growth factor (VEGF) is the main inductor of angiogenesis, the procedure of development of new vessels. Nox4, the main isoform of NADPH oxidase, predominates in the endothelial cells of the retina. This results in the generation of hydrogen peroxide instead of other reactive species. Hydrogen peroxide can play the role of a signaling molecule in the VEGF signaling molecule. Upregulation of expression Nox4 with catalase expression downregulation and/or activities in diabetes increases the concentration of hydrogen peroxide which promotes neovascularization of the retina through the VEGF signaling pathway. In a study on a diabetic rat model, a high concentration of hydrogen peroxide was observed in retinal cells, creating oxidative stress conditions inside the cell. Because retinal cells have a high content of polyunsaturated fatty acids, they can be oxidized by hydroxyl radicals generated by Fenton's hydrogen peroxide reaction. High levels of lipid peroxide and damage to oxidative DNA were observed in diabetic retinopathy (87-90). In a recent study, researchers were able to distinguish between five different clusters of diabetes by combining parameters such as insulin resistance, insulin secretion, and measurements of blood sugar levels with age onset of the disease. Group 1 essentially corresponds to type 1 diabetes, while type 2 diabetes is further divided into four subgroups marked as group 2 to group 5. Individuals with insulin secretion disorders and moderate insulin resistance are labeled under group 2 (severe group of diabetes with insulin deficiency), while group 3 included severe patients with insulin-resistant diabetes with obesity and severe insulin resistance. Group 4 consists of mild obese diabetes patients who are obese and fall ill at a relatively young age, while the largest group of patients is in the group 5 with mild age-related diabetes in mostly elderly patients. The relationship between this new classification of diabetes with catalase expression levels or its activity has not yet been investigated for communication, if any, and needs further research.3.2. Neurological disorders3.2.1. Alzheimer's DiseaseAlzheimer is one of the onset of dementia disease in adults (92). According to a report by the Alzheimer's Association, about 5.5 million people in the United States suffer from Alzheimer's disease in 2017. By 2050, the prevalence of Alzheimer's disease is expected to increase significantly from 4.7 million in 2010 to about 13.8 million in 2050. Many factors, including smoking and diabetes, with a higher risk of developing dementia. Alzheimer's disease is characterized by deposition of senile plaques of amyloid β in the brain (94, 95). There are several studies that show that β peptides are toxic to neurons in culture (96-109). Amyloid β, a product of amyloid precursor protein (APP), is a soluble component of plasma and cerebrospinal fluid (CSF). In all cases of Alzheimer's disease, it has been observed that soluble amyloid β converted into insoluble fibrillation in senile plaques by forming protein-protein adduks (96-99, 101). It has been observed using in vitro cell culture research that the nascent amyloid β is non-toxic, but at the age of amyloid β becomes toxic to neurons. It has been observed that amyloid peptide β is responsible for the accumulation of hydrogen peroxide in cultures of neuroblastoma and hippocampus neurons (111, 112), probably by directly binding amyloid β with catalase, which leads to a decrease in enzyme activity. These findings led to the development of the hypothesis that catalase-amyloid β interaction may play a significant role in the incremental hydrogen peroxide in cells linking amyloid accretion β and the development of oxidative stress conditions in Alzheimer's disease. Thus, the current hypothesis about the mechanism of amyloid β-stimulated oxidative damage in cells is that amyloid β directly interacts with catalase by binding to the protein and deactivating its catalytic activity, thus creating oxidative stress conditions. In addition, full-length amyloid β peptides bind to Cu2 in their N-terminal peptide and reduce it to the shape of Cue. It has been reported that the amyloid complex β-Cue can lead to the production of hydrogen peroxide (114, 115). Thus, catalase has both a direct and indirect relationship with the pathogenesis of Alzheimer's disease.3.2.2. Parkinson's diseaseParkinson is an age-related neurological disorder with an initial symptom like simple arm tremor that gradually affects all body movement, reducing quality of life seriously with the progression of the disease. Its clinical manifestations include bradynesia, stiffness, resting tremor and postural instability. It starts with rhythmic tremor of the limbs, especially during periods of rest or sleep. At the stage of the disease, patients face difficulties in controlling movement and muscle stiffness. This causes muscle stiffness, slow motion and slowness of initiation. The disease is characterized by dopamine depletion due to damage to dopamine-producing neurons in substantia nigra pars compacta (SNpc) (116-118). It has been demonstrated that Parkinson's disease-affected patients suffer from 100-200 SNpc neuronal damage per day. Because various factors such as genetic inheritance, environmental toxins, oxidative stress and mitochondrial likely to participate in the disease, it is very difficult to understand the pathogenesis of Parkinson's disease. It has been demonstrated that the protein, alpha (α) of sine (sine, is closely related to cytopatology and histopathology of Parkinson's disease). It has been observed that mutation in the gene responsible for the production of α-synuclein leads to the production of a mutant protein that can contribute to the deposition of dopamine in the cytoplasm of neurons. Small neurotransmitter molecules, such as dopamine, are synthesized in the cytoplasm and transmitted to small bubbles as they oxidize in physiological pH. Mutant α-sinecline permeates these bubbles, causing dopamine to leak into the cytoplasm, where it autooxidizes the production of hydrogen peroxide, superoxide molecules and toxic dopamine-quinone species, creating oxidative stressful conditions. Mutant α-sineclein protein is known to also inhibit the expression and activity of catalase. Arrest of catalase activity α-sineklein probably prevents peroxysom-activated receptor γ (PPAR) transcription activity, which regulates the expression of the CAT gene. Based on such experiments, it can be concluded that low catalase activity and high production of hydrogen peroxide in Parkinson's disease can be caused by (indirect) inhibition of catalase expression by a molecule α-synuclein.3.3. Vitiligo Vitiligo is one of the chronic pigment disorders where the cells of the skin's melanocytes - the pigment responsible for skin color - are

damaged or unable to produce melanin. Various studies have shown that the level of catalase in the epidermis of patients with vitiligo is lower compared to the level of healthy control subjects (124, 125) with the result of increased concentration of hydrogen peroxide. In the cell, hydroxyl radicals can be produced spontaneously from hydrogen peroxide through photochemical contraction, i.e. Haber-Weiss reactions. These hydroxyl radicals are able to oxidize lipids in the cell membrane. This may cause damage to keratinocytes and melanocytes in the epidermal layer of the skin in such patients (126-130). In addition, the inhibitory effect of hydrogen peroxide or modification of the PPC gene leads to low catalase activity. However, it has been noted that there is an unsustainable link between catalase polymorphism and vitiligo. Polymorphisms 389C/T Exon 9, Codon 389 and -89A/T promoter region were studied in patients with vitiligo (34, 44, 46, 47, 131, 132). However, the results were not marked as consistent. Among the Chinese population, the association was observed in AT and TT genotypes with an increased risk of vitiligo while no association was observed between vitiligo and -89A/T CAT polymorphism in the Korean population (34, 44). In the case of polymorphism 389C/T, several studies showed no difference between vitiligo administers and patients (34, 44, 46, 131) contrasting results were also obtained in several studies (47, 131). It has been reported that a mutation in the CAT gene can alter gene expression and/or cause structural changes in keratinocytes and/or melanocytes. Although the results are incompatible with demographic studies, the relationship between pathogenesis and catalase may still be possible, as disparate demonstrations are reported in the literature. Therefore, further research is needed to understand the link.3.4. AcatalasemiaAcatalasemia (AC) is a hereditary disorder that is associated with an abnormality of the enzyme catalase affecting its activity. In 1948, Takahara, a Japanese otolaryngologist, first reported the disorder (133, 134). He found that four of the seven races in Japan had the same genetic flaw. His ex vivo experiments consisted of filling an ulcer in a patient's mouth with hydrogen peroxide. Since no bubble formation was observed, he concluded that catalase or its enmistic activity was absent in the saliva of patients. In honor of its main findings, this disease was baptized as Takahara's disease. Acatalashemium and hypocatalasia mean gomozygates and heterozygates, respectively. Heterozygota acatalazemia shows half of catalase activity than usual, and this phenotype is known as hypocatalazemia. Depending on the geographical location from where it was first studied, there are different types of acatalsemia described as Japanese, Swiss, Hungarian, German and Peruvian types. To date, about 113 akatharasemic patients from all over the world have been registered. Two types of mutations in the catalase gene are reported to be involved in Japanese acatalazemia. The merging of the mutation was prosecuted for Japanese acatalassemia I, where the replacement of guanine residues with adenine residues at 5 intron 4 disrupted the splicing of the RNA product that produces the defective protein. In Japanese acatalsemia II, the frame shear mutation occurs due to the removal of thymine at 358 exon 4, which alters the amino acid sequence and produces a new TGA codon (stop) at 3 terminals. The translation of this mutated filament produces polypeptide from 133 amino acid residues. It is a truncated protein that is unstable and non-functional. Aebi et al. was first described as Swiss acatalasesemia (139-141 years). A study of fibroblast from Swiss acatalase patients suggests that structural mutations in the CAT gene are responsible for catalase inactivation. Gough, a Hungarian biochemist, first described Hungarian acatalsesemia in 1992 after studying the disease in two Hungarian sisters. It found that catalase activity in the blood of these two acatalazemic sisters had 4.4% and 6.7% of the reference catalase activity in a healthy population while the activity rate in hypocatalasic patients was 38.9% (24). Research in his lab led Gotta to suggest that THE CAT gene and, as a result, structural changes in the catalase protein are responsible for Hungarian acatalazemia. This laboratory also reported that there is a risk of diabetes among Hungarian members of the acatalasemic family although further biochemical and genetic analysis should be performed to test the hypothesis that acatalazemic patients are more likely to develop diabetes. There are usually four types of Hungarian acatalsemia, which varies depending on the (different) place of the gene mutation in the DNA. The same is true in Table 3.4. The therapeutic role of catalase is one of the most important antioxidant enzymes. As it decomposes hydrogen peroxide into harmless products such as water and oxygen, catalysis is used against numerous oxidative diseases associated with stress as a therapeutic agent. The difficulty in applying remains in the delivery of the catalase enzyme to the appropriate place in sufficient quantities. Poly (milk coglycolic acid) nanoparticles have been used to deliver catalase to human neuronal cells, and the protection of these catalase-loaded nanoparticles from oxidative stress has been evaluated. It was noted that the effectiveness of catalase encapsulation was very high with approximately 99% of enzymatic enmeptic activity encapsulated catalase along with significantly sustained activity during the month. The nanoparticles loaded with catalase have shown significant positive effects on neuronal cells pre-exposed to hydrogen peroxide reduction hydrogen peroxide-mediated protein oxidation, DNA damage, mitochondrial membrane transition of opening pores, and loss of membrane integrity. Thus, the study shows that nanoparticles loaded with catalase can be used as a therapeutic agent in oxidative stress-related neurological diseases. Similar studies have been conducted using EUK 134, which is a class of synthetic superoxide dismutase /mimetic catalase as an effective therapeutic agent for stroke. EUK 134 is a salen-manganese complex that has both high catalase and superoxide dismutase activity. From these studies, based on the rat stroke model, it was concluded that EUK 134 could play a protective role in the fight against the disease. Studies using Tat-CAT and 9Arg-CAT fusion proteins as therapeutics have also been conducted with encouraging results. To study the effects of these synthesis proteins in conditions of oxidative stress, the mammalian cell lines (HeLa, PC12) were transduceable with the purified synthesis of Tat-CAT and 9Arg-CAT protein, and these cells were exposed to hydrogen peroxide. It was found that the viability of trans induced cells increased significantly. It has also been noted that when Tat-CAT and 9Arg-CAT protein synthesis were sprayed on animal skin, it could penetrate the epidermis and dermis layers The fusion proteins transfuzed in mammalian cells were active enzymatically for more than 60 hours, after which they became unstable. This study shows that these fusion proteins may be is used as a protein therapeutic agent for catalase-related disorders. Amyotrophic lateral sclerosis (ALS) is one of the most common types of progressive and fatal neurological disorders, leading to the loss of motor neurons mainly in the spinal cord as well as to some extent in the motor cortex and brain stem. Among the two different types of ALS, the family form (FALS) accounts for 10% of all ALS cases and 15 to 20% of FALS cases are associated with a mutation of the SOD1 gene, an antioxidant enzyme that purifies superoxide radical. In some cases, FALS has been found to have a mutation in the SOD1 gene not related to the reduced activity of SOD1. Rather, mutated SOD1 has toxic properties without reducing enzymatic activity. This mutated SOD1 protein reacts with some abnormal substrates, such as hydrogen peroxide, using it as a substrate, and produces the most reactive hydroxyl radical, which can seriously damage important biomolecules. Mutated SOD1 also has the potential to use peroxinitrite as an atypical substrate, leading to the formation of 3-nitrothyroid, which leads to the conversion of functional protein into a non-functional one. Catalase can reduce the concentration of hydrogen peroxide by detoxifying it. Therapeutic approaches have also been taken using catalase, modified putrescin, in the treatment of FALS. It was found that putrescine-catalase-polyamine modified catalysis-delayed progression weakness in the FALS transgenic mouse model. Thus, the delay in the development of clinical weakness in transgenic mice FALS makes catalase, modified by putrescin, a good candidate as a therapeutic agent for diseases associated with catalase anomaly. In this regard, it should be noted that putrescin-modified catalysis reportedly has an extended function of permeability of the gemmozeo-brain barrier, while maintaining its activity comparable to that of native catalase with pristine delivery to the central nervous system after parenteral administration. Therefore, further research with this molecule seems to be justified. Studies were conducted using synthetic mymetic SOD catalase, increasing the lifespan of FILA stranded SOD2 mice along with recovery from spongy encephalopathy and relieving mitochondrial defects. These findings lead the authors to the hypothesis that SOD-catalase of mimetic may be used as a potential therapy for various neurological diseases associated with oxidative stress, such as Alzheimer's disease and Parkinson's disease. Studies using diabetic mice such as type 1 and type 2 with 60-fold controlled catalase expression have shown improved cardiomyocyte function. Cardiomyopathy is associated with the improper functioning of the heart muscles where the muscles enlarged, thick or stiff. This can lead to irregular heartbeats or heart failure. Many diabetic patients suffer from cardiomyopathy with structural and functional anomalies without the presentation of concomitant coronary heart disease or hypertension. As mentioned, catalase is associated with the pathogenesis of diabetes. It has been observed that a 60-fold increase in catalase activity can drastically reduce the usual features of diabetic cardiomyopathy in the mouse model. Due to the overexpression of catalase, morphological disorders of mitochondria and myofibrilla of the heart tissue were prevented. The breakdown of cardiac contracting was also inhibited by a decrease in the production of reactive oxygen, mediated by high glucose concentrations. Thus, this approach may be an effective therapeutic approach for the treatment of diabetic cardiomyopathy. The future PerspectiveThis review summarizes the link between catalase and the pathogenesis of certain critical diseases such as diabetes, Parkinson's disease, catalalusemia, vitiligo and Alzheimer's disease. More attention needs to be paid to the role of catalase in the pathogenesis of stress-related oxidative diseases and its therapeutic approach. Catalase plays an important role in the metabolism of hydrogen peroxide as a key regulator (28, 29, 152-154). Some studies have also shown the involvement of catalase in controlling the concentration of hydrogen peroxide, which is also involved in the signaling process .155-158. Acatalazemia is a rare genetic disease that is not as devastating as other diseases discussed here, but it may be a mediator in the development of other chronic diseases due to prolonged oxidative stress on the tissue. We also discussed the risk of type 2 diabetes among akatharasemic patients. But more research is needed on the biochemical, molecular and clinical aspects of the disease. There are still many questions about a catalassemia and its relationship to other diseases that need to be answered. Therefore, further research is needed to focus on the mutations of the catalase gene and its association with acatalazema and other diseases with reduced catalase activity, so that the link can be understood more fully. Therapeutic approaches using catalase require more experimental testing so that clinical trials can be initiated. Using catalase as a medicine or therapy can be a new and broad area of study. Any new finding about the therapeutic use of catalase will have a huge contribution to medical science. Positive results may be directed to its possible use for the treatment of various oxidative diseases associated with stress.6 ConclusionCatalase is one of the most important antioxidant enzymes that plays an important role in splitting hydrogen peroxide and maintaining cellular redox homeostasis. Diabetes, Alzheimer's disease, Parkinson's disease, etc. are now becoming common diseases. While there are many factors involved in the pathogenesuse of these diseases, several studies from various laboratories have shown that has to do with the pathogeness of these diseases. Research into this is many scientists in various laboratories have explored various aspects of these diseases, but with an ever-increasing ageing population, much remains to be done. On the other hand, the potential of catalase as a therapeutic drug in the treatment of several stress-related oxidative diseases is not adequate and is still being studied. More research is needed to confirm if catalase can be used as a drug in the treatment of various age disorders. The authors state that they have no conflict of interest. Recognitions Lighteners thank the Council of Scientific and Industrial Research (CSIR), India (Project 38 (1343)/12/EMR-II) for EMR grants. AN is grateful to the CSIR for the Project Scholarship and the University Grants Commission (UGC), India, for a non-NET scholarship. Additional materials (Additional Figure 1). In module 1 ACOX1 (peroxysomal akinzym oxidase), HSD17B4 (peroxysoma multifunctional enzyme) and HAO1 (hydroxyacid oxidase 1) are involved in the oxidation pathway of fatty acids in peroxysomem, while DAO protein (D amino acidic oxidation) is involved in the metabolism of amino acids in peachsis. All components of Module 1 are involved in various metabolic pathways. Proteins in module 2 are mainly involved in responses to oxidative stress. All proteins have antioxidant activity, with the exception of AKT1 (RAC-alpha serin-trionin protein kinase). AKT1 is a serin-trionin protein called kinase that is involved in cell survival, metabolism, growth, and angiogenesis. All proteins of both modules 1 and 2, including CPR, have catalytic activity and are located in the lumen of intracellular organelles. SOD2 and AKT1 modules 2, including CAT, were involved in the regulatory path of longevity and the SIGNALing pathway of FOXO in mammals (additional numbers 2 and 3). But in many other species, SOD1 and SOD3 (superoxide dismutase 3) were also involved along with SOD2, AKT1, and PPC (Additional Figure 4). Among reactive types of hydrogen peroxide is free diffusion and relatively long-term. It acts as a weak oxidation as well as a decrease in the agent; However, it is not very reactive, but it is the progenitor of many other reactive oxygen types (ROS). It has been demonstrated to oxidize glyceraldehyde-3-phosphate dehydrogenase by oxidizing the sexual main groups of thyol in the active location of this enzyme. In most cellular injuries, this molecule is known to play an indirect role. One of the most important products is the formation of a more reactive free radical ·OH sweeping in the presence of the transition of metal ions such as Fe2 using the Fenton reaction.