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Properties of the urease enzyme as a component of self-healing concrete. Review

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Abstract:

Urease is a thermally stable metal enzyme that plays a critical role in ecosystems and industrial processes, particularly in the production of self-healing concrete. In nature, the enzyme catalyzes the hydrolysis of urea, providing mineralization of nitrogen and increasing its bioavailability for plants, which contributes to maintaining fertility and sustainability of ecosystems. Urease is actively involved in the metabolism of soil microorganisms, improves the decomposition of organic residues, and optimizes ammonia emission, which reduces the risk of environmental pollution. With unique properties such as thermal stability, high catalytic activity, and urea specificity, urease finds application in various fields of human activity, from medical diagnostics to microbiological cementation. The article provides an overview of the biochemical and molecular features of the urease enzyme that are relevant for use in building materials technologies. The analysis of the main posttranslational modifications of the enzyme and environmental factors affecting the structure, properties, and functions of urease in pro- and eukaryotic organisms is presented.

1 Introduction

Urease (urea amidohydrolase, code CF 3.5.1.5) is a cytosolic hydrolytic enzyme containing a two–core nickel metal center that catalyzes the decomposition of urea to form ammonia and carbon dioxide [1], [2], [3], [4].

The enzyme's activity was first discovered in 1876 by French chemist Frederic Alphonse Musk, who isolated it from urine. The urine ammonia fermentation occurs due to an enzyme that can act in the absence of a living organism. The discovery confirmed the general hypothesis regarding all fermentations, which was demonstrated by Eduard Buchner in 1897 in the case of alcoholic fermentation [5], [6], [7].

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The urease could be crystallized by cooling a solution containing purified urease and acetone. He also experimentally proved that purified urease is a protein. Sumner's work was the first demonstration that a protein could function as an enzyme and eventually led to the recognition that most enzymes are actually proteins. Urease was the first crystallized enzyme, and D. Sumner was awarded the Nobel Prize in Chemistry in 1946 [8], [9].

Two nickel ions are present in the active center of the bean urease. The presence of two nickel ions is necessary for bean urease catalytic activity [10], [11].

In the period 2019-2024, 128 studies on urease activity and its properties were published, 7 of which are of a review nature, and 121 research articles. The factors influencing urease activity in the composition of building materials have also been studied in many studies.

Despite numerous successful laboratory studies, research conducted under construction conditions remains limited due to the complexity of the hydration process and the high alkalinity of cement-based materials.

Decrees are widespread metalloenzymes produced by plants, fungi, and bacteria, as well as some animals, such as drosophila *(Drosophila melanogaster)*, French snail (*Helix pomatia)*, and northern elephant hare (*Aplysia californica*). Urease plays a key role in nitrogen metabolism and is used in various fields, from ecology and medicine to industry [12], [13], [14], [15], [16].

2 The Literature Search Methods

When writing the article, the bibliographic databases Google Scholar, Scopus, PubMed (National Center for Biotechnology Information), Science Direct, and the database of the Russian Science Citation Index were used. The search for works on the topic was carried out no later than 2002, with rare exceptions (section introduction), which highlights the history of the discovery of urease.

Examples of keywords, phrases, and search queries: urease, urease discovery, urease activity, bio-concrete, urease genes, biochemical properties of urease, urease evolution, urease thermal stability, etc.

3 Literature Review

3.1 Classification and molecular structure of urea

Urease subgroup or urea amidohydrolase (classification enzyme number 3.5.1.5) belongs to the class of hydrolases. The urease subclass is hydrolases acting on ether bonds. The urease groups are amidhydrolases and phosphotriesterases. According to the type of protein, they are a heteromer consisting of three different subunits (α, β, γ), the cofactor of enzyme activity is nickel ions (Ni^{2+}). Urease can have different isoforms depending on the body. Thus, ureases are members of the superfamily of amidohydrolases and phosphotriesterases, which, with some exceptions, contain two Ni^{2+} ions in their active centers. The molecular weight of the enzyme averages 480,000 atomic mass unit (AMU). [17], [18], [19], [20].

The active center of the cut is located in the α subunits and is a bis-μ-hydroxo-dimeric center with an interatomic distance between nickel ions approximately equal to 3.5 angstroms. Nickel ions, in turn, are connected by carboxylated lysine. The active center of ureases consists, in addition to two nickel atoms, of one carbamylated lysine, four histidines, and one aspartate residue**.**

Water molecules are present in the active center of the enzyme. During the catalytic reaction, the water molecule is split into a hydroxide ion and a proton. The hydroxide ion then attacks the carbonyl group of urea, which leads to its cleavage into ammonia and carbon dioxide [21], [22].

(1)

The hydroxide ion then attacks the urea [21]:

(2)

These reactions are key to urease's functioning and allow the enzyme to catalyze the cleavage of urea effectively. The hydroxide ion connects two nickel atoms, which, together with three water molecules, form a tetrahedral cluster of water with hydrogen bonds in the active center. Nickel ions can protect urease from free radical damage by binding to potentially active oxygen molecules and preventing their interaction with oxidation-sensitive amino acid residues [23], [24], [25], [26].

The following active processes occur in the active urease site:

Urea binds to nickel ions through its carbonyl and amide groups, forming a complex with an active center.

One of the nickel ions coordinates the water molecule, facilitating its deprotonation to form a hydroxyl ion.

The hydroxyl ion attacks the carbonyl group of urea, leading to the formation of an intermediate carbamate.

Carbonate decomposes to form ammonia and carbon dioxide [18], [23], [27], [28], [29], [30], [31], [32].

This process can be represented in detail in the form of the following chemical equations [11].

(3)

(4)

Amino acids surrounding nickel ions, such as histidine (His), aspartate (Asp), and glutamate (Glu), help to stabilize intermediate states and substrates. For example, a histidine residue can act as a base, taking a proton from water and thereby contributing to the formation of an active hydroxyl ion [11], [17], [33], [34].

The structure of the active urease center is optimized for efficient catalysis, making urease one of the most powerful and effective enzymes. This allows the body that produces it to efficiently process urea, which is part of its nitrogen metabolism [11].

The primary amino acid sequences of ureases, regardless of origin, are identical in 55% of cases. The number of polypeptide chains forming a **functional unit** (monomer) varies depending on the source of the enzyme. Plant and fungal ureases are characterized by a single polypeptide chain (α, 60-76 kDa). The most common structure of plant ureases is the dimer of trimers $(\alpha_3)_2$; however, dimeric/trimeric/tetrameric ureases of plants and fungi have been described [31,35,36].

The functional unit of bacterial ureases is formed by two subunits (α and β, 8-21 kDa, found to date in the genus Helicobacter – ([αβ]3)4, with α, 26-31 kDa, β, 61-66 kDa) or three (α, β and γ, 6-14 kDa) types of polypeptide chains. Bacterial cuts are often trimers ([αβγ]3). The amino acid sequences of the smaller subunits of prokaryotic ureases coincide with the corresponding site in the single chain of eukaryotic ureases [11], [37], [38], [39], [40].

The molecular structure of urease may differ slightly between organisms, but the general principle of the organization of subunits remains [1].

Each subunit plays an important role in ensuring the structural integrity and catalytic efficiency of the enzyme:

The α subunit (alpha, size varies from species, often up to 80 kDa) is key since it is here that the active site of the enzyme is located and the catalytic reaction takes place. In the active center, urea is hydrolyzed to ammonia and carbon dioxide. The amino acid sequence of the α subunit varies depending on the organism and determines its three-dimensional structure and functional properties. The genes encoding the α subunit (igeA) are often located in the urease operon (excluding eukaryotes) and are regulated in response to the concentration of urea in the medium. The α subunit can be modified to increase thermal stability, which is important for industrial applications of the enzyme. The α subunit interacts with the β and γ subunits, ensuring proper assembly and functioning of the urease [39], [40], [41], [42], [43].

The β subunit (beta, size varies from species, often up to 66 kDa) plays an important role in the structural organization of the enzyme, helping to maintain the three-dimensional structure of urease, which is important for its catalytic activity [44]. It is known that the β subunit interacts with the α subunit, helping to form the active center of the enzyme and ensuring its stability. The β subunit also interacts with the γ subunit, which contributes to the proper assembly of the enzymatic complex. The genes encoding the β subunit (ureB) are also, as in the case of α, they are located in the operon and can be regulated together with other components of the enzyme. The β subunit may be a target for immobilization or chemical modification in order to increase the stability and activity of urease for industrial purposes and may participate in the regulation of urease activity in response to changes in environmental conditions [44], [45].

The gamma subunit (gamma, size varies from species, often up to 20 kDa) is one of the three subunits that make up the heterotrimeric urease complex. The γ subunit helps to stabilize the quaternary structure of the enzyme, which is critically important for its activity. It is important to note that although

the γ subunit itself is not catalytically active, it contributes to the formation of the active center of the enzyme in cooperation with the α and β subunits and participates in interactions that ensure proper assembly and, therefore, functioning of the urease. The gene encoding the γ subunit (igeS), is usually located in the same operon as the genes for the α and β subunits and is regulated along with them. In studies to improve the properties of urease, the γ subunit can be modified to increase thermal stability and protect against denaturation [20], [46], [47], [48].

Based on the molecular features, the structural diversity of urease is due to several factors. Firstly, functional units often form larger complexes, such as trimers, hexamers, multimers, and dodecamers. The three-dimensional structure of urease, in turn, is determined by the sequence of amino acids and can vary depending on the source of the enzyme, which affects its thermal stability and catalytic properties. Secondly, the location and coordination of nickel ions differ in the ureases of different organisms. For example, in the urease of

The main PTMs affecting the structural features and variations of ureases:

Acetylation of lysine residues or the N-terminus of a protein leads to a decrease in positive charge or a change in charge, which alters the interaction between protein chains. Acetylation can reduce the protein's stability, making it more sensitive to high temperatures [52], [53].

Phosphorylation, i.e., the addition of a phosphate group to serine, threonine, or tyrosine, can cause conformational changes. These changes may increase or decrease the stability of the enzyme depending on the site of modification or its interaction with regulatory proteins [54], [55].

Methylation of arginine and lysine residues increases the protein's hydrophobicity by changing its conformation or interaction with regulatory proteins. Increased hydrophobicity may contribute to protein stability at high temperatures [56], [57], [58], [59].

Nickel plating, i.e., coordination of nickel ions with histidine and carboxylate groups in the active center of urease, with the formation of a metal center. This coordination strengthens the structure of the active center, making it less susceptible to thermal denaturation [60], [61].

Glycosylation, i.e., the addition of sugar residues to asparagine serine or threonine. Although glycosylation is more often associated with eukaryotic proteins, some bacteria are also able to glycosylate their proteins, including urease, which affects the protection of the enzyme from proteolytic cleavage [56,62,63].

Ubiquitination, or the process of attaching the ubiquitin protein to lysine residues. Ubiquitination can regulate the activity or stability of urease. In eukaryotes, this mechanism often serves as a signal for enzyme degradation in the proteasome. In animals, ubiquitination affects the enzymes of the urea cycle involved in nitrogen metabolism [64].

Sulfation, i.e., the addition of a sulfate group to tyrosine, may affect the interaction of urease with glycosaminoglycans or other proteins. This process can change the charge and hydrophilicity of tyrosine residues and affect their stability. However, the specific role of sulfation in the regulation of urease activity requires additional study [65], [66], [67].

One specific example of a bacterium in which PTM ureases have been studied is *Helicobacter pylori*. This bacterium uses urease to survive in the acidic environment of the human stomach. The urease of *Helicobacter pylori* undergoes several PTMs that help it adapt to an acidic environment, namely nickel plating, acetylation, and phosphorylation [54], [55], [60], [68]. Studies of these modifications help to understand how Helicobacter pylori adapts to the gastric environment and contribute to the development of new treatments for infections caused by this bacterium [69], [70].

Thus, PTMs play an important role in determining the structure of ureases, their activity, interaction with other proteins and molecules in the cell, and the thermal stability of the enzyme, especially in environmental conditions where temperature can vary greatly

3.2 The mechanism of action and main functions of urea amidohydrolase

Ureases catalyze the hydrolysis of urea into ammonia and carbamic acid (which is then decomposed into another ammonia molecule and carbon dioxide). Thus, the first function of ureases, based on the mechanism of action, is catalytic. Various factors, including substrate concentration, the presence of inhibitors or activators, and physico-chemical environmental conditions, can regulate urease activity. It was found by using computer modeling that the efficiency of the reaction in the presence of urease is 10.32 times higher than the theoretical rate of non-catalyzed hydrolysis of urea (without taking into account the restrictions imposed by the diffusion of the substrate in water) [13], [17], [31], [71], [72], [73], [74], [75], [76].

As noted earlier, the main mechanism of action is concentrated in the active centers of α subunits and includes several stages. Initially, urea enters the active center and binds to nickel ions, which leads to a weakening of the bond between the carbon atom and nitrogen atoms in the urea molecule. Next, the hydroxyl group (OH^-) binds to one of the nickel ions and attacks urea, leading to the formation of an intermediate carbamate. The carbamate is then hydrolyzed to ammonia and carbon dioxide. This process is accompanied by the transfer of a proton from water to a urea molecule, which contributes to the rupture of the C-N bond. The resulting ammonia is released, and the active center returns to its original state, ready for a new cycle of catalysis [11], [72], [77].

It is important to note that different ureases may have different regulatory mechanisms and PTMs that affect their activity and stability. For example, bacterial ureases are often regulated through the availability of nickel ions and can be inhibited by various substances such as fluorides or heavy metals. The main urease inhibitors are considered to be Pb2+ ions and other heavy metals, hydrogen peroxide, and acetohydroxamic acid. It has been established that reactivation of urease inhibited by heavy metals is possible when interacting with ethylenediaminetetraacetic acid [78], [79], [80], [81].

The pH value also plays an important role in the realization of the main catalytic function and activity of the enzyme. pH affects the ionic state of amino acid residues in the active site, which can alter the enzyme's ability to bind substrate or cofactors such as nickel ions. It is worth noting that the pH of the medium can affect the charge of the urea molecule and other molecules interacting with urease, which can change the efficiency of binding and hydrolysis. Acidic or highly alkaline conditions can cause enzyme denaturation. It is known that the average optimal pH value for all types of ureases is 7-8 [82]. At the same time, prokaryotes usually have ureases with an optimal pH range of about 7.0–7.5 [83], [84], which can be extremely resistant to pH changes and allow them to function in a variety of conditions. In eukaryotes, including plants and fungi, ureases can have a wider range of optimal pH values, often from 5.0 to 8.0 [85]. Eukaryotic ureases can also be adapted to the conditions of the environment in which they are expressed and may have different regulatory mechanisms. Urease activity can be adapted to the conditions of the environment in which they function. For example, ureases found in acidic soil may be more resistant to acidic conditions than ureases found in neutral or alkaline environments [86], [87], [88].

The regulatory function is to maintain nitrogen balance. Ammonia formed as a result of urease activity is often used directly by microorganisms or can be converted into other nitrogen compounds such as nitrates or amino acids. The regulation of ureases in the nitrogen cycle highlights their importance for maintaining nitrogen balance in various biological ecosystems [1], [72], [89].

In addition to the significant role of urease in nitrogen metabolism, the non-catalytic properties of this enzyme are also known. Ureases, well known as virulence factors, due to ammonia production and alkalinization in diseases of urease-positive microorganisms, have anti-inflammatory, endocytosis-inducing, and neurotoxic activity in living organisms such as Helicobacter pylori, Klebsiella pneumoniae, Yersinia pestis, and Schistosoma mansoni. It is especially important for plants that ureases have insecticidal and fungitoxic effects. Data on a recombinant peptide obtained from plant urease have shown that interaction with lipids of cell membranes can be the basis of nonenzymatic biological properties of ureases [1], [90], [91], [92].

3.3 Thermal stability as a distinctive property of urease

One of the main properties facilitating the technological application of urease is its thermal stability. Thermal stability is the ability of an enzyme to maintain its activity at high temperatures. The optimum operating temperature of the urease is 60 °C [93], [94], [95].

Of course, this property is determined by the molecular features of the enzyme structure:

1. It has been found that thermostable ureases usually have a more compact three-dimensional structure, which reduces the likelihood of denaturation at high temperatures. In practice, protein engineering can be used to create additional disulfide bridges in urease, which increases structural stability and thermal stability [94], [96], [97].
2. Strengthening hydrogen bonds and optimizing solvation can increase heat resistance and stabilize the enzyme structure. For example, mutations that increase the number of hydrogen bonds within a protein can help urease withstand higher temperatures [82], [85].
3. An increase in the content of nickel ions in the active center can increase the enzyme's thermal stability [98].

4. It has been found that replacing amino acids with more hydrophobic ones or those that form more stable interactions can improve thermal stability. For example, replacing lysine with arginine in certain positions increases stability at high temperatures [99].

As well as external environmental conditions or targeted effects on the enzyme:

1. The addition of certain cofactors or chemical modifiers can increase the thermal stability of urease. Magnesium and calcium ions can interact with negatively charged groups on the protein's surface, increasing its stability at high temperatures [100].
2. Mutagenesis, i.e., the use of directed action to create mutants with increased thermal stability [101], [102].
3. Immobilization, which is carried out by fixing urease on nanoparticles, can increase its thermal stability and protect it from thermal denaturation [103].
4. The addition of polymers or polyols such as glycerin can stabilize the enzyme and prevent its denaturation at high temperatures [104], [105].
5. The optimal pH (described earlier) and salt composition of the medium can contribute to the thermal stability of urease, reducing thermal denaturation and preserving protein conformation [85,98].
6. Urease genes derived from extremophilic organisms (Bacillus pasteurii, Bacillus subtilis), which naturally produce proteins resistant to high temperatures, can be used to produce thermostable enzymes [106], [107], [108], [109].

All these urease features and strategies can be used to increase the thermal stability of urease, which expands its scope of application in various fields, including biocementation and bioremediation [114], [115], [116]. The thermal stability of urease allows the enzyme to be effective even at high temperatures. This thermal stability makes it possible to apply urease in various climatic zones and contributes to the sustainable development and environmental safety of products obtained with the help of the enzyme.

3.4 Urease genes and regulation of their activity

Urease genes encode both the enzyme of the same name and related proteins, and may include several exons and introns, the location of which depends on the type of organism. Urease genes exhibit significant conservatism among different species. This conservatism indicates their fundamental role in nitrogen metabolism. However, there are also species-specific differences that may reflect adaptation to certain ecological niches [110], [111], [112], [113].

In prokaryotes, as a rule, urease genes are located in the nucleoid and organized into operons, which include several genes necessary for the synthesis of an active enzyme and the transport of urea into the cell. The structure of the urease operon usually contains three structural genes, designated as ureA, urea, and ureC. Urease genes encode the corresponding subunits of the enzyme. In addition, additional genes such as red, urea, urea, urea, and ureH may be present, involved in the assembly of the active center of the enzyme and the insertion of nickel ions [114], [115], [116], [117].

Urease gene expression is carefully regulated at several levels, including transcriptional, post-transcriptional, and post-translational regulation. This regulation allows cells to adapt to changes in nitrogen availability and other environmental conditions. Prokaryotes often regulate the expression of urease genes at the transcription level in response to the concentration of urea in the environment. For example, regulatory proteins (UreR) are present in the bacteria of the genus Helicobacter and Klebsiella. UreR proteins activate the transcription of the urease operon at high concentrations of urea. The expression of urease genes can also be regulated at the mRNA level, for example, through mRNA stability or translation efficiency. Urease activity can be regulated through modifications of the protein after its synthesis, including the addition or removal of metal ions from the active center. The expression of prokaryotic urease genes is regulated in response to urea concentration and pH of the medium. For example, in bacteria of the genus Helicobacter, urease helps to maintain an optimal pH for the survival of bacteria in the acidic environment of the stomach. Prokaryotic urease genes and their regulation play a key role in nitrogen metabolism. The expression level of urease genes can be regulated in response to the concentration of urea and ammonia in the environment, which allows microorganisms to adapt to changes in nitrogen availability [118], [119], [120], [121], [122].

Urease genes in eukaryotes, although similar to prokaryotic ones in their function, may have differences in organization and regulation. Urease in eukaryotes also catalyzes the cleavage of urea to ammonia and carbon dioxide. Still, the mechanisms of regulation of these genes may be more complex

due to the characteristics of eukaryotic cells. Urease genes in eukaryotes can be located in different places of the genome, depending on the type of organism. For example, in plants that have urease activity, urease genes can be found in nuclear, chloroplast, and mitochondrial DNA. In nuclear DNA, these genes can be part of larger genetic blocks called gene families. In plants such as soy (Glycine max), urease genes may be located on different chromosomes. For example, in the soybean genome, the Eu1 urease gene is located on chromosome 8, and the Eu4 gene is located on chromosome 21 [50], [110], [120], [123], [124], [125], [126], [127], [128], [129], [130], [131].

The main eukaryotic urease genes are URE1, which encodes urease in many eukaryotes, including yeast. The URE2 and URE3 genes, and in some cases, additional genes associated with urease, are involved in regulating its activity or transport [117], [132], [133], [134], [135].

The expression of eukaryotic urease genes can be activated or suppressed in response to changes in the concentration of urea or other nitrogen sources. Transcription factors such as NIT2 in some fungi can bind to promoters of urease genes and regulate their transcription. DNA methylation and histone modifications can alter the structure of chromatin, thereby regulating the availability of urease genes for transcription factors. This altering of the structure can lead to long-term changes in gene expression. microRNAs and other noncoding RNAs can interact with urease mRNAs, affecting their stability or translation. Alternative splicing can also generate different urease isoforms, which may have different properties or localization in the cell. Phosphorylation, ubiquitination, and other modifications can regulate the activity, stability, or interaction of urease with other proteins. It is important to note that, as in prokaryotes, urease activity in eukaryotes depends on the pH of the medium [136], [137], [138], [139], [140], [141], [142].

3.5 The evolution of ureases

It is assumed that the first ureases could have arisen in anaerobic conditions, where urea served as an important source of nitrogen. There are several hypotheses regarding the origin of urease. One hypothesis suggests that urease could have arisen as a result of genetic duplication and subsequent divergence from other ancient enzymes that catalyzed similar reactions. This arisening could have happened in the anaerobic conditions of the ancient oceans, where urea and other organic compounds served as important sources of nitrogen [3], [110], [113], [143], [144].

Nitrogen is a key element for the synthesis of amino acids and nucleotides necessary for the further construction of proteins and nucleic acids. Over time, urease underwent structural changes that improved its ability to bind to urea and catalyze its cleavage. These changes are reflected in the three-dimensional structure of the enzyme, which determines its activity and specificity [124], [145], [146].

Urease is shared among various groups of organisms, including bacteria, fungi, plants, and some invertebrates. This sharing indicates that urease originated in the early stages of evolution and was preserved as a result of horizontal gene transfer or convergent evolution. Urease has acquired various functions depending on the body. For example, in plants, it participates in nitrogen metabolism; in some bacteria, it helps to survive in an acidic environment; and in many marine organisms, urease plays a role in regulating osmotic pressure [113], [143], [147].

In the course of evolution, urease genes could undergo changes that allow organisms to adapt to different environmental conditions. Urease genes are subjected to selection pressure, which can stimulate the preservation of the basic functions of the enzyme while at the same time initiating changes that can improve functionality or adaptability in new conditions [153], [154].

The main aspects of the genetic evolution of urease:

1. Random mutations in DNA could lead to changes in the amino acid sequence of urease, which improves or worsens its functional properties. It was found that the missense mutation (A354V) alanine substitution for valine at position 354 can increase hydrophobicity near the active center and affect substrate binding; nonsense mutation (Q279), i.e. the introduction of a stop codon at position 279 leads to premature termination of translation and the formation of a shortened version of the enzyme; insertion (Ins GGGG at position 201-202) insertion of four nucleotides between codons 201 and 202 leads to a shift in the reading frame and a change in the subsequent amino acid sequence and properties of the enzyme; deletion (F310), i.e. removal of phenylalanine at position 310 can change the conformation of the protein and its activity[148], [149], [150], [151], [152], [153].
2. Duplication of the genes encoding urease could lead to the appearance of additional copies of the enzyme. These duplications allowed one copy of the genes to retain its original function and the other copy to adapt to new conditions[120], [154].

3. Urease genes can be transferred between different species through horizontal gene transfer, which promotes the spread of the enzyme among various organisms [11], [155].

4. Organisms with more adapted genetic variants of urease have an advantage in survival and reproduction, which leads to the preservation and spread of beneficial genetic variants [3], [143], [156], [157], [158], [159].

5. It has been established that not only the structural genes of urease but also the regulatory elements controlling its expression can evolve. This evolution allows the enzyme to respond more accurately to changes in the environment [70], [82], [160], [161], [162].

Studying the genetic evolution of urease helps scientists understand how enzymes adapt to changes in the environment and what mechanisms underlie their evolution. Currently, this knowledge can be used to create more efficient and stable versions of enzymes for industrial applications, including biobetone and other biotechnological processes.

3.6 Applied use of urease activity

Due to their unique properties, ureases have found wide application in industry, diagnostics, and biotechnology.

Scope of application of urease:

1. Agriculture. Urease genes are used to create transgenic plants that can more effectively use urea as a fertilizer. This allows for a reduction in the consumption of nitrate fertilizers and environmental pollution [24], [44], [163], [164].

2. Medicine. Urease tests are used to diagnose infections caused by Helicobacter pylori, a bacterium that causes human stomach ulcers. They help to quickly detect the presence of bacteria in the gastrointestinal tract [165].

3. Bioremediation. Microorganisms, which produce urease, are widely used in this industry. Urease genes are used to create microorganisms capable of purifying wastewater from urea and other nitrogen-containing compounds, which prevents reservoir eutrophication [166], [167].

4. Biobetone or microbiological cementing. In construction, microorganisms carrying urease genes are used to create a material that regenerates itself due to microbial activity. Microorganisms that produce urease contribute to the hardening of calcium in cracks. The thermal stability of the enzyme allows the use of foam concrete in extreme climatic conditions [168], [169], [170], [171]. Bacteria are mainly used for the production of self-healing concrete, but the first works have appeared suggesting the use of fungi of the genus Trichoderma [172].

5. Production of bioplastics. The use of urease genes can help produce biopolymers such as polyhydroxyalkanoates (PHAS), which are biodegradable and environmentally friendly alternatives to traditional plastics [173], [174], [175].

6. Food industry. Urease can improve the properties of products in the food industry. For example, it can reduce the urea content in wines and cheeses, improving their taste and safety [95], [176], [177], [178].

Thus, urease is widely used in various industries. However, the development and optimization of urease applications requires a careful approach and consideration of the specifics of the processes and conditions in each case.

4 Conclusions

With distinctive properties such as thermal stability, high catalytic activity, and urea specificity, urease finds application in various fields of human activity, from medical diagnostics to microbiological cementation. The article provides an overview of the biochemical and molecular features of the urease enzyme that are relevant for use in building materials technologies.

Conclusions:

1. The study of urease functions and mechanisms of action opens up new horizons for understanding complex interactions in nature and contributes to practical application in various scientific and industrial fields.

2. Evolutionary changes in amino acid sequences and the structure of the enzyme's active center ensured its adaptation to specific ecological niches. Modern biotechnological methods allow genetic modification of ureases, which improves their thermostable properties, increases their catalytic activity, and changes their specificity. These modifications open up new areas of application of urease in

medicine, agriculture, and environmental technologies (bioremediation, production of degradable biopolymers).

3. Urease plays a key role in improving the properties of foam concrete by participating in biomineralization processes. Combining the catalytic activity of urease with the technological capabilities of concrete opens up new opportunities in the construction industry, contributing to the creation of more sustainable, durable, and environmentally friendly materials.

4. Thus, optimization of fermentation conditions and improvement of urease application techniques can significantly increase the efficiency of processes that contribute to sustainable development and improve the quality of life.

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