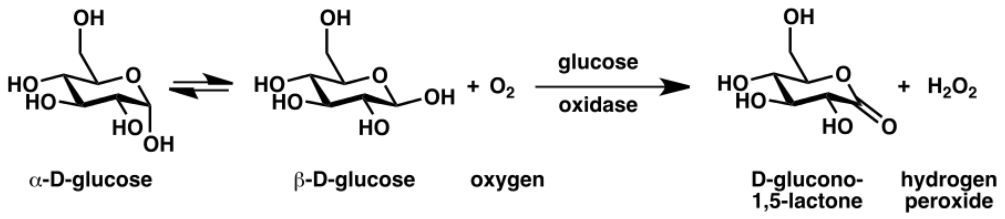
Glucose oxidase

The **glucose oxidase** enzyme (**GOx** or **GOD**) also known as **notatin** (EC number 1.1.3.4) is an oxidoreductase that catalyses the oxidation of glucose to hydrogen peroxide and D-glucono-δ-lactone. This enzyme is produced by certain species of fungi and insects and displays antibacterial activity when oxygen and glucose are present.[2]



Reaction catalyzed by glucose oxidase

Glucose oxidase is widely used for the determination of free glucose in body fluids (medical testing), in vegetal raw material, and in the food industry. It also has many applications in biotechnologies, typically enzyme assays for biochemistry including biosensors in nanotechnologies.[3][4] It was first isolated by Detlev Müller in 1928 from *Aspergillus niger*.[5]

Contents

Function

Several species of fungi and insects synthesize glucose oxidase, which produces hydrogen peroxide, which kills bacteria.[2]

Notatin, extracted from antibacterial cultures of *Penicillium notatum*, was originally named **Penicillin A**, but was renamed to avoid confusion with penicillin.[6] Notatin was shown to be identical to **Penicillin B** and glucose oxidase, enzymes extracted from other molds besides *P. notatum*;[7] it is now generally known as glucose oxidase.[8]

Early experiments showed that notatin exhibits *in vitro* antibacterial activity (in the presence of glucose) due to hydrogen peroxide formation.[6][9] *In vivo* tests showed that notatin was not effective in protecting rodents from *Streptococcus haemolyticus*, *Staphylococcus aureus*, or salmonella, and caused severe tissue damage at some doses.[9]

Glucose oxidase is also produced by the hypopharyngeal glands of honeybee workers and deposited into honey where it acts as a natural preservative. GOx at the surface of the honey reduces atmospheric O_2 to hydrogen peroxide (H_2O_2), which acts as an antimicrobial barrier.[10]

Structure

GOx is a dimeric protein, the 3D structure of which has been elucidated. The active site where glucose binds is in a deep pocket. The enzyme, like many proteins that act outside of cells, is covered with carbohydrate chains.

Mechanism

At pH 7, glucose exists in solution in cyclic hemiacetal form as 63.6% β-D-glucopyranose and 36.4% α-D-glucopyranose, the proportion of linear and furanose form being negligible. The glucose oxidase binds specifically to β-D-glucopyranose and does not act on α-D-glucose. It oxidises all of the glucose in solution because the equilibrium between the α and β anomers is driven towards the β side as it is consumed in the reaction.[3]

Glucose oxidase catalyzes the oxidation of β-D-glucose into D-glucono-1,5-lactone, which then hydrolyzes into gluconic acid.

In order to work as a catalyst, GOx requires a coenzyme, flavin adenine dinucleotide (FAD). FAD is a common component in biological oxidation-reduction (redox) reactions. Redox reactions involve a gain or loss of electrons from a molecule. In the GOx-catalyzed redox reaction, FAD works as the initial electron acceptor and is reduced to $FADH^-$.[11] Then $FADH^-$ is oxidized by the final electron acceptor, molecular oxygen (O_2), which can do so because it has a higher reduction potential. O_2 is then reduced to hydrogen peroxide (H_2O_2).

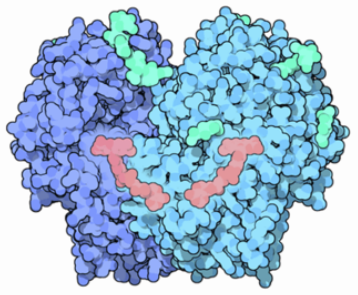
Applications

Glucose monitoring

Glucose oxidase is widely used coupled to peroxidase reaction that visualizes colorimetrically the formed H_2O_2, for the determination of free glucose in sera or blood plasma for diagnostics, using spectrometric assays manually or with automated procedures, and even point-of-use rapid assays.[3][8]

Similar assays allows the monitoring of glucose levels in fermentation, bioreactors, and to control glucose in vegetal raw material and food products. In the glucose oxidase assay, the glucose is first oxidized, catalyzed by glucose oxidase, to produce gluconate and hydrogen peroxide. The hydrogen peroxide is then oxidatively coupled with a chromogen to produce a colored compound which may be measured spectroscopically. For example, hydrogen peroxide together with 4 amino-antipyrene (4-AAP) and phenol in the presence of peroxidase yield a red quinoeimine dye that can be measured at 505 nm. The absorbance at 505 nm is proportional to concentration of glucose in the sample.

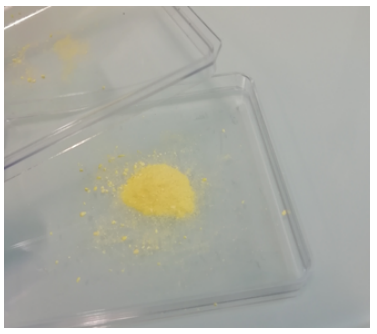
Glucose oxidase



Structure of glucose oxidase dimer (dark and light blue) complexed with FAD (salmon) and glycans (aquamarine) from *Penicillium amagasakiense*.[1]

Identifiers	
EC no.	1.1.3.4 (https://www.qmul.ac.uk/sbcs/iubmb/enzyme/EC1/1/3/4.html)
CAS no.	9001-37-0 (http://www.commonchemistry.org/ChemicalDetail.aspx?ref=9001-37-0&title=)
Databases	
IntEnz	IntEnz view (https://www.ebi.ac.uk/intenz/query?cmd=SearchEC&ec=1.1.3.4)
BRENDA	BRENDA entry (http://www.brenda-enzymes.org/enzyme.php?ecno=1.1.3.4)
ExPASy	NiceZyme view (https://enzyme.expasy.org/EC/1.1.3.4)
KEGG	KEGG entry (https://www.genome.jp/dbget-bin/www_bget?enzyme+1.1.3.4)
MetaCyc	metabolic pathway (https://biocyc.org/META/substring-search?type=NIL&object=1.1.3.4)
PRIAM	profile (http://priam.prabi.fr/cgi-bin/PRIAM_profiles_CurrentRelease.pl?EC=1.1.3.4)
PDB structures	RCSB PDB (https://www.rcsb.org/search?q=rcsb_polymer_entity.rcsb_ec_lineage.id:1.1.3.4) PDBe (https://www.ebi.ac.uk/pdbe/entry/search/index?ec_number:1.1.3.4) PDBsum (https://www.ebi.ac.uk/thornton-srv/databases/cgi-bin/enzymes/GetPage.pl?ec_number=1.1.3.4)
Gene Ontology	AmiGO (http://amigo.geneontology.org/amigo/term/GO:0046562) / QuickGO (https://www.ebi.ac.uk/QuickGO/term/GO:0046562)
Search	
PMC	articles (https://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&term=1.1.3.4%5BEC/RN%20Number%5D%20AND%20pubmed%20pmc%20local%5Bsb%5D)
PubMed	articles (https://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&term=1.1.3.4%5BEC/RN%20Number%5D)
NCBI	proteins (https://www.ncbi.nlm.nih.gov/protein?term=1.1.3.4%5BEC/RN%20Number%5D)

Enzymatic glucose biosensors use an electrode instead of O_2 to take up the electrons needed to oxidize glucose and produce an electronic current in proportion to glucose concentration.[12] This is the technology behind the disposable glucose sensor strips used by diabetics to monitor serum glucose levels.[13]



Glucose oxidase enzyme powder from *Aspergillus niger*.

Food preservation

In manufacturing, GOx is used as an additive thanks to its oxidizing effects: it prompts for stronger dough in baking, replacing oxidants such as bromate.[14] It is also used as a food preservative to help remove oxygen and glucose from food when packaged such as dry egg powder to prevent unwanted browning and undesired taste.[15]

Wound treatment

Wound care products, such as "Flaminal Hydro" make use of an alginate hydrogel containing glucose oxidase and other components as an oxidation agent.

Clinical trials

A nasal spray from a bag-on-valve device that mixes glucose oxidase with glucose has undergone clinical trials in 2016 for the prevention and treatment of the common cold.[16][17][18]

See also

- Oxidoreductase
- Glucose meter

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18. Clinical trial number *NCT01883453 (https://www.clinicaltrials.gov/show/NCT01883453)* for "A Nasal Spray With Glucose Oxidase as a Treatment of Common Cold" at ClinicalTrials.gov

External links

- "Glucose Oxidase: A much used and much loved enzyme in biosensors" (https://web.archive.org/web/20040820162613/http://www-biol.paisley.ac.uk/marco/enzyme_electrode/chapter3/chapter3_page1.htm) at University of Paisley
- Glucose+Oxidase (https://meshb.nlm.nih.gov/record/ui?name=Glucose%20Oxidase) at the US National Library of Medicine Medical Subject Headings (MeSH)