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Установлено, что дикультуры синезеленых водорослей (*A. laxa + T1 Anabaenopsis* и *Anabaenopsis sp. (T1) + Sph.Zetterstedtii*) характеризуются повышенной скоростью роста и накоплением биомассы по сравнению с монокультурами. Предполагается, что это связано с возникновением мутуалистических взаимоотношений между видами микроводорослей.

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It is found that blue-green algae dicultures (*A.laxa + Anabaenopsis sp.* T1 strain and *Anabaenopsis sp.* T1 strain + *Sph.Zetterstedtii*) are characterized by high growth and accumulation of biomass compared to monocultures. It is supposed that this is connected with the occurrence of mutualistic relationships between species of microalgae.

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## XENOBIOTIC TRANSFORMING ACTIVITY OF ANIMAL MOLYBDOENZYMES

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Most the attention to date in metabolism of drugs and foreign compounds has been focused on the microsomal monooxygenase system. This system plays an important role in the oxidation of aromatic carbocyclic compounds. However, the presence of the one ore more nitrogen atoms in the aromatic ring makes heterocyclic compounds also susceptible to oxidation via a second group of enzymes known as the "molybdenum hydroxylases". These cytosolic enzymes, which include xanthine oxidase (XO, EC 1.2.3.2) and aldehyde oxidase (AO, EC 1.2.3.1), form a closely related group with similar molecular properties but differ some what in substrate specificity. Both enzymes are also involved in some physiological processes and also the metabolism of some endogenous compounds which may indicate their important roles in *in vivo* conditions [2].

These enzymes are metalloflavoproteins that catalyze both oxidation and reduction of a broad range of drugs and other xenobiotics indicating the importance of these enzymes in drug oxidation, detoxification and activation. Xanthine oxidoreductase (XOR) appears in two interconvertible forms xanthine dehydrogenase (XDH), and xanthine oxidase (XO). Xanthine oxidoreductase catalyzes the hydroxylation of hypoxanthine to xanthine and of xanthine to urate. Oxidative hydroxylation occurs at the molybdenum center. With XDH $NAD^+$ is reduced; with XO molecular oxygen is reduced at the flavin center. Molybdenum-containing hydroxylases catalyze the hydroxylation of carbon centers using oxygen derived ultimately from water, rather than $O_2$, as the source of the oxygen atom incorporated into the product, and do not require an external source of reducing equivalents.

The relative importance of these two groups of oxidative enzymes is illustrated by comparing the *in vitro* oxidation of several bicyclic ring system. Naphtalene is oxidized via the microsomal monooxygenase system to an unstable epoxide intermediate which ultimately gives rise to a mixture of 1-naphtol and 2-naphtol. However, naphthalene is not a substrate for the molybdenum hydroxylases. Quinoline, 1-azanaphtalene, reacts not only with the microsomal enzyme system but also with aldehyde oxidase to give a number of mono- and dihydroquinolines with rabbit or rat liver fractions. As the number of N atoms in the molecule increases, the molybdenum hydroxylases play a more dominant role in the oxidative biotransformation of these compounds. Thus, quinazoline, 1,3-diazanaphtalene, is rapidly oxidized by both aldehyde oxidase and xanthine oxidase to quinazolin-4-one, whereas only small amounts of phenolic microsomal products can be detected. Furthermore, quinazolin-4-one is subsequently converted to quinazolin-2, 4-dione by the molybdenum hydroxylases. Finally pteridine, 1,3,5,8-tetraazanaphtalene, is oxidized in vitro via the molybdenum hydroxylases only; xanthine oxidase converts it sequentially to pteridin-2,4,7-trione, whereas it is converted to pteridin-2,4-dione by aldehyde oxidase.

The reason for the change in emphasis from microsomal oxidation of naphthalene to the molybdenum hydroxylase catalyzed attack of pteridine is due to the additive activating effect of each nitrogen atom toward nucleophilic attack of the ring system. The molybdenum hydroxylases catalyze a reaction which involves attack by a nucleophile. Therefore, oxidation normally occurs at the carbon atom adjacent to a ring nitrogen,

which is generally the most electropositive carbon. The oxygen atom incorporated into the substrate is ultimately derived from water. In contrast, the microsomal monooxygenase system catalyzes electrophilic attack involving molecular oxygen, and the carbons in the heterocyclic rings are deactivated toward electrophilic reagents. The two reactions can be presented thus [2]:

$RH + OH^- \rightarrow$ aldehyde oxidase, xanthine oxidase $\rightarrow ROH + 2e^- + H^+$

$RH + O_2 + NADPH + H^+ \rightarrow$ monooxygenases $\rightarrow ROH + H_2O + NADP^+$

The molybdenum hydroxylases function by being alternately reduced by the substrate (RH) and reoxidized by molecular oxygen (or $NAD^+$) under physiological conditions. In addition to the two atoms of molybdenum, these enzymes also contain two molecules of FAD per mole of enzyme. Both superoxide anion and hydrogen peroxide are produced via either one-electron or two-electron transfer. These pathways can be illustrated by the following equation:

$FADH_2 + 2O_2 \rightarrow FAD + 2H^+ + 2O_2^-$

$FADH_2 + O_2 \rightarrow FAD + H_2O_2$

Reactions catalyzed by molybdoenzymes. AO and XO oxidize the oxidation of a wide range of heterocyclic compounds. Although the enzymes have similar molecular properties, their substrate specificities are quite different, with regard to both rate of oxidation and the position of attack. However, the role of these enzymes in the oxidation of drug-derived aldehydes has not been established. The investigation described the interaction of eleven structurally related benzaldehydes with guinea pig liver aldehyde oxidase and bovine milk xanthine oxidase, since they have similar substrate specificity to human molybdenum hydroxylases. The compounds under test included mono-hydroxy and mono-methoxy benzaldehydes as well as 3,4-dihydroxy-, 3-hydroxy-4-methoxy-,4-hydroxy-3-methoxy-, and 3,4-dimethoxy-benzaldehydes. In addition, various amines and catechols were tested with the molybdenum hydroxylases as inhibitors of benzaldehyde oxidation. The kinetic constants have shown that hydroxy-, and methoxy-benzaldehydes are excellent substrates for aldehyde oxidase with lower affinities for xanthine oxidase. Therefore, aldehyde oxidase activity may be a significant factor in the oxidation of the aromatic aldehydes generated from amines and alkyl benzenes during drug metabolism. In addition, amines acted as weak inhibitors, whereas catechols had a more pronounced inhibitory effect on the aldehyde oxidase activity. It is therefore possible that aldehyde oxidase may be critical in the oxidation of the analogous phenyl acetaldehydes derived from dopamine and noradrenaline.

There are very few monocyclic substrates of these enzymes; pyridine and its diaza analogues, pyrimidine, pyrazine and pyridazine, do not react with the molybdoenzymes *in vitro*. However, some substituted pyridines and pyrimidines are metabolized, and these examples emphasize the difference in substrate specificity between the AO and XO.

XO catalyses nitrite reduction to nitric oxide under anaerobic conditions [1]. The XO reducing substrate xanthine, NADH, triggered nitrite reduction to NO, and the molybdenum-binding XO inhibitor oxypurinol inhibited this NO formation, indicating that nitrite reduction occurs at the molybdenum site. Nitrite and reducing substrate concentrations were important regulators of XO-catalyzed NO generation. It is well known that in mammals including humans, NO is an important cellular signaling molecule involved in many physiological and pathological processes. XO-catalyzed nitrite reduction can be an important source of NO generation under ischemic conditions [5].

It was suggested that XO is an inducible enzyme and that treatment of mice with xanthine results in elevation of enzyme levels. Similarly, when phtalazine, a substrate of both molybdoenzymes, is administrated to rabbits an increase in the activity of each enzyme is observed. The "induced" AO differs from the control enzyme in some physico-chemical properties. It was also shown that that hydralazine, a substituted phtalazine, is an inhibitor of rabbit AO activity both *in vivo* and *in vitro*. XO activity is not altered by hydralazine. Interesting results are obtained when the carcinogen 2-acetylaminofluorene is administered to rats. XO activity increases, as does one isozyme of AO, however, the second isozyme is absent from induced liver.

The molybdenum hydroxylases are widely distributed throughout the animal the plant and animal kingdoms. Two detailed studies comparing the occurrence of aldehyde oxidase and xanthine oxidase in more than 100 species have shown that these enzymes are present, either separately or together, in species as diverse as the sea anemone and man. Species differences in the levels of aldehyde oxidase are more pronounced than those of xanthine oxidase, with herbivores containing the highest levels of former enzyme. Aldehyde oxidase levels appear to be comparatively low in humans.

Levels of both enzymes are high in mammalian liver although xanthine oxidase is present in similar concentrations in lactating mammary tissue and small intestine, and concentrated 1000-fold in bovine milk lipid globules.

Sulfite oxidase, (EC 1.8.3.1) third molybdoenzyme is an enzyme in the mitochondria of all eukaryotes. It oxidizes sulfite to sulfate and, via cytochrome c, transfers the electrons produced to the electron transport chain, allowing generation of ATP in oxidative phosphorylation.

The recently discovered mammalian fourth molybdenum containing protein mARC1 is capable of reducing N-hydroxylated compounds. It was named mARC because the N-reduction of amidoxime structures was initially studied using this isolated mitochondrial enzyme. Upon reconstitution with cytochrome $b_{(5)}$ and $b_5$ reductase, benzamidoxime, pentamidine, and diminazene amidoximes, N-hydroxymelagatran, guanoxabenz, and N-hydroxydebrisoquine are efficiently reduced. These substances are amidoxime/N-hydroxyguanidine prodrugs, leading to improved bioavailability compared to the active amidines/guanidines. Thus, the recombinant enzyme allows prediction about in vivo reduction of N-hydroxylated prodrugs. Furthermore, the prodrug principle is not dependent on cytochrome P450 enzymes [3].

All hitherto analyzed mammalian genomes harbor two mARC genes: molybdenum cofactor (Moco) sulfurase C-terminal domain MOSC1 and MOSC2. Proteins encoded by these genes represent the simplest eukaryotic molybdenum enzymes, in that they bind only the Moco. It is also suggested that they are members of a new family of molybdenum enzymes. mARC and its N-reductive enzyme system plays a major role in drug metabolism, especially in the activation of so-called "amidoxime-prodrugs" and in the detoxification of N-hydroxylated xenobiotics, though its physiological relevance is largely unknown [4].

Thus, molybdenum is an essential trace element for virtually all life forms. It functions as a cofactor for a number of enzymes that catalyze important chemical transformations in the global carbon, nitrogen, and sulfur cycles. At least 50 molybdenum-containing enzymes are now known in bacteria, plants and animals. Thus, molybdenum-dependent enzymes are not only required for the health of the Earth's people, but for the health of its ecosystems as well. Humans require very small amounts. Plants are common sources of molybdenum for animals and human. However, the amount of molybdenum in plants varies with how much is in the soil.

Linxian is a small region in northern China where the incidence of cancer of the esophagus and stomach is very high (10 times higher than the average in China and 100 times higher than the average in the U.S. The soil in this region is low in molybdenum and other mineral elements, so dietary molybdenum is also low. Increased intake of nitrosamines, which are known carcinogens, may be one of a number of dietary and environmental factors that contributes to the development of gastroesophageal cancer in this population. Plants require molybdenum to synthesize nitrate reductase, a molybdoenzyme necessary for converting nitrates from the soil to amino acids. When soil molybdenum content is low, plant conversion of nitrates to nitrosamines increases, resulting in increased nitrosamine exposure for those who consume the plants. Adding molybdenum to the soil in the form of ammonium molybdenate may help decrease the risk of gastroesophageal cancer by limiting nitrosamine exposure.

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## ОЦЕНКА УСТОЙЧИВОСТИ ГЕНОТИПОВ ПШЕНИЦЫ К СВИНЦУ И ЦИНКУ ДЛЯ СОЗДАНИЯ ЭКОЛОГИЧЕСКИ ЧИСТОЙ ТЕХНОЛОГИИ ЕЕ ВОЗДЕЛЫВАНИЯ

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*В настоящей работе представлена оценка устойчивости к свинцу и цинку различных генотипов озимой пшеницы в лабораторных условиях. Проведенный скрининг позволил выявить устойчивые и чувствительные формы.*

Наиболее острая проблема, решение которой имеет практическое значение, является загрязнение тяжелыми металлами агроценозов вблизи крупных промышленных центров. Отдельные сорта различных видов продовольственных культур проявляют существенные различия по устойчивости к