CNEU MEDICAL s.r.o.
Jeřábkova 1459/8, Chodov, 149 00 Praha 4, Czech Republic

Analysis of possible interference factors in reagent (CarciReagent)

(Literature research according to the standard EN 13612: 2002)

No.: APIF/ZYB/2021

Introduction

Aims of this research paper is to carry out a literature search in accessible scientific publications and find out, according to the categories (Interfering drugs that may cause false positive test results, Interfering drugs that may cause false negative test results, Interference factors of diet, Human body's own interference factors, Interfering factors of physical diseases, Diseases associated with abnormal tyrosine metabolism), the factors of possible affecting the level of monohydroxyphenol metabolites in the patient's urine in order to eliminate false negative or false positive results CarciReagent test. This information will be used for recommendation inside of product user leaflet.

Content:

1, Name of in vitro diagnostic device for self-testing
2, Description of in vitro diagnostic device for self-testing
3, Intended use of in vitro diagnostic device for self-testing
4, Principle and function of in vitro diagnostic device for self-testing
5, Objective of literature research for functional evaluation of in vitro diagnostic device for self-testing
6, Plan of literature research for functional evaluation of in vitro diagnostic device for self-testing
6a, Responsible person of literature research for functional evaluation of in vitro diagnostic device for self-testing
6b, Timetable for literature research for functional evaluation of in vitro diagnostic device for self-testing
6c, Design of literature research for functional evaluation of in vitro diagnostic device for self-testing
6d, Key words of literature research for functional evaluation of in vitro diagnostic device for self-testing
7, Structure of literature research for functional evaluation of in vitro diagnostic device for self-testing
7.1, Interfering drugs that may cause false positive test results
7.2, Interfering drugs that may cause false negative test results
7.3, Interference factors of diet
7.4, Human body's own interference factors
7.5, Interfering factors of physical diseases
7.6, Diseases associated with abnormal tyrosine metabolism
8, Literature research conclusion
9, User manual recommendation (interference factor part)
10, References and list of documents

CNEU MEDICAL s.r.o.
Jeřábkova 1459/8, Chodov, 149 00 Praha 4, Czech Republic

1, Name of in vitro diagnostic device for self-testing
CarciReagent

2, Description of in vitro diagnostic device for self-testing
Test kit for the detection of the approximate amount of monohydroxyphenol metabolites (tyrosine) in urine (Lay semi-quantitative test for self-testing) (Chemical chromogenic method)

3, Intended use of the in vitro diagnostic device for self-testing
"CarciReagent - an in vitro diagnostic device for self-testing, intended for the detection of monohydroxyphenol metabolites (tyrosine) and its approximate amount in the patient's urine (Lay semiquantitative test)"

4, Principle and function of in vitro diagnostic device for self-testing
The basic principle of the test is based on the improved method of Millon's reagent (Millon's reagent), which monitors the increased amount of tyrosine (monohydric phenolic amino acids and their metabolites) in the urine. By changing the color of the mixture in the ampoule after adding 3 ml of morning urine (middle urine stream), the reaction color cascade can be used to determine if urine samples contain increased amounts of these metabolites. The reagents in the ampoule and the tyrosine content in the urine show a characteristic chromogenic response that can be used for the clinical diagnosis of intracellular metabolic abnormalities (detection of possible changes or disorders in metabolism within the human cell). The determined approximate content of tyrosine in urine (according to the attached table from 0–2000 mg per liter of urine) reacts with the chemical reagent and, depending on its amount, turns colored. According to the enclosed color scale, the test result can be read from No. 1 to No. 8. The result from No. 1 to No. 3 is the amount of tyrosine in the normal concentration, so the result is considered negative, and no increased amount of tyrosine has been demonstrated. With results No. 4 and No. 5, it is already a positive finding of an increased amount of tyrosine in the urine. If the tyrosine concentration is higher than 500 mg per liter of urine, ie result No. 6, No. 7, No. 8, this is a positive result, a high content of tyrosine in the urine may indicate a more serious disease. In case of positive results, it is recommended to perform a more thorough examination by a general practitioner in order to exclude the risk of a possible serious illness.

5, Objective of literature research for functional evaluation of in vitro diagnostic device for self-testing
Aims of this research paper is to carry out a literature search in accessible scientific publications and find out the factors of possible affecting the level of monohydroxyphenolmetabolites in the patient's urine in order to eliminate false negative or false positive results of CarciReagent test.

6, Plan of literature research for functional evaluation of in vitro diagnostic device for self-testing
6a, Responsible person of literature research for functional evaluation of in vitro diagnostic device for self-testing
Huang Ganhui (Professor at Nanchang University)

6b, Timetable for literature research for functional evaluation of in vitro diagnostic device for self-testing
1.9-30.9.2021

6c, Design of literature research for functional evaluation of in vitro diagnostic device for self-testing

This literature research is about the factors of possible affecting the level of monohydroxyphenol metabolites in the patient's urine according to the categories include: Interfering drugs that may cause false positive test results, Interfering drugs that may cause false negative test results, Interference factors of diet, Human body's own interference factors, Interfering factors of physical diseases, Diseases associated with abnormal tyrosine metabolism.

6d, Key words of literature research for functional evaluation of in vitro diagnostic device for self-testing

Key words: tyrosine, tyrosinase, thyroid, melanin, melanoma, carcinoma, dopamine, urine, amino acid metabolites, tumors, malignant

7, Structure of literature research for functional evaluation of in vitro diagnostic device for self-testing

7.1 Interfering drugs that may cause false positive test results

If the patient takes certain drugs that cause changes in the body´s metabolism, the test results may be falsely positive, such as peptides and hormone drugs, traditional Chinese medicine, central nervous system drugs, amino acids, etc., specifically:

7.1.1 Some hormone drugs mainly include:

7.1.1.1 Thyroid hormone drugs, thyroid hormone is a derivative of iodinated tyrosine.

References:

1. Thyroid hormone drugs. (Refer to the webpage to see the "thyroid hormone drugs" entry on Baidu Encyclopedia - https://baike.baidu.com/item/%E7%94%B2%E7%8A%B6%E8%85%BA%E6%BF%80%E7%B4%A0%E7%B1%BB%E8%8D%AF%E7%89%A9/16999330?fr=aladdin

2. Zhang Ying, Zhang Feng, Zhang Xiangdong. 3,5-Dimethyl-DL-tyrosine synthesis research. Journal of Liaoning University Natural Science Edition, 2007, 34 (1), 74 - 77. https://kns.cnki.net/kcms/detail/detail.aspx?dbcode=CJFD&dbname=CJFD2007&filename=LNDZ200701021&v=v0fLi53uYHMPKUnCNkMzYuQDf%25mmd2B5MMcwW7c6GtJr9atQx1lTRh0RnsG%25mmd2BTo7fndQuH

7.1.1.2 Catecholamine hormone drugs are synthesized from phenylalanine and tyrosine.

References:

3. Catecholamine hormones (Refer to the webpage to see the "Catecholamine Hormones" on Baidu Encyclopedia - https://baike.baidu.com/item/%E5%84%BF%E8%8C%B6%E9%85%9A%E8%83%BA%E7%B1%BB%E6%BF%80%E7%B4%A0

7.1.1.3 Corticosteroids and glucocorticoid drugs, such as hydrocortisone.

References:

4. Liu Zhijun, Tang Xianhua. The effect of corticosteroids on melanin synthesis in human A375 melanoma cell line. The 18th National Academic Conference on Dermatology and Venereology, Chinese Medical Association, 2012, 6, 470
https://kns.cnki.net/kcms/detail/detail.aspx?dbcode=CPFD&dbname=CPFD0914&filename=ZHYX201206006595&v=%25mmd2BuTG1qga74kG6mGvGkQQVbqeW%25mmd2FylOM8Ty2jd%25mmd2BQKp6yP6UZ2z2KL%25mmd2BkxeARy9JSS4OUZ0rYjKYomY%3d

5. Lu Jian, Xu Renbao, Dong Rongchun. Glucocorticoid receptor of human hepatocellular carcinoma cell line (SMMC-7721) and induction of tyrosine aminotransferase by glucocorticoid. Journal of Experimental Biology, 1985, 18 (2): 231 - 236.
https://kns.cnki.net/kcms/detail/detail.aspx?dbcode=CJFD&dbname=CJFD8589&filename=SWSB198502010&v=ts1cgz60INhGT6YGqNMwxMBC%25mmd2BRY1NAPW1s%25mmd2Bj5n76M%25mmd2F5Z3z5U3FrTukrTicqS7UDi

6. Deng Ruichun, Zhou Yong, Zhang Jingang, etc. The effect of hydrocortisone on tyrosinase and melanogenesis of B-16 melanoma cells. Chinese Pharmacological Bulletin, 2002, 18 (4), 433-436.
https://kns.cnki.net/kcms/detail/detail.aspx?dbcode=CJFD&dbname=CJFD2002&filename=YAOL200204019&v=kBj7lm%25mmd2Bs1ZYHnblH9H82rx5U4XYyEoWCjrRLGzTLooomsagiLttWYjmt7qzTcWv5

7.1.2 Ethanol extracts in some Chinese medicines can significantly activate the activity of tyrosinase, including: Salvia miltiorrhiza, Polygonum multiflorum, Huang Cen, Dandelion, Honeysuckle, Amomum villosum, Chinese wolfberry, Hawthorn, Prunella vulgaris, Cuscuta, Qianghuo, Star anise, Poria, Atractylodes, White front, Black snake, Gastrodia, Patchouli, Bupleurum, Ligustrum , Ligustrum lucidum, Plum blossom, Wang Buliuxing, Tongcao, Ganoderma lucidum, Polyporus umbellatus, Panax notoginseng, Alisma, Sanleng, Pork tooth soap, 8-Methoxypsoralen, and the compound Chinese medicine "Vitiligo Granule" etc.

References:

7. Wang Jianhua, Lei Fan, Hu Bo. Study on the Activation of Tyrosinase by 10 Kinds of Chinese Medicines. Chinese Journal of Information on Traditional Chinese Medicine, 2000, 7 (4), 40.
https://kns.cnki.net/kcms/detail/detail.aspx?dbcode=CJFD&dbname=CJFD2000&filename=XXYY200004024&v=HbVrK3gv95IgIGBhkK%25mmd2Bl1uo9mC%25mmd2F5xbFpPsfAxHPJOKX7%25mmd2BM6WuOSWDrygDZ%25mmd2BfWkTo

8. Wu Lifeng, Cai Yujie, Liao Xiangru, etc. The activation of tyrosinase in ethanol extracts of 45 traditional Chinese medicines, Natural Products Research and Development, 2011, 23:517-521.
https://kns.cnki.net/kcms/detail/detail.aspx?dbcode=CJFD&dbname=CJFD2011&filename=TRCW201103030&v=DRy%25mmd2FMhC7DRAGGzl8ftbmqxdt1CFSYYVeTCUMyB1ysgXMKFRhjL%25mmd2BSSqye0xN37iPQ

9. Wen Renqing, Lu Weihong, Yan Chunxia, etc. Basic and clinical research on the relationship between tyrosinase activity and melanogenesis. Chinese Aesthetic Medicine, 2014, 12 (23), 2028-2031.
https://kns.cnki.net/kcms/detail/detail.aspx?dbcode=CJFD&dbname=CJFDLAST2015&filename=MRYX201423033&v=W0DGelHvuS4g8p%25mmd2F6osAwG8Ab6NwRvEHhTaiPXXP2KbO%25mmd2FBV2Cv91RAcUYU7aJYNnK

10. Liu Jingye, Liu Tao. Effects of psoralen on tyrosinase activity and melanin synthesis of human melanocytes. Skin Diseases and Venereal Diseases, 2019, 41(3): 322-325.
https://www.cnki.com.cn/Article/CJFDTotal-PFBX201903008.htm

7.1.3 Some neurological drugs used to treat Parkinson's disease, such as dopamine-like drugs, levodopa tablets, are mainly composed of spindopa. Chemical name: 3-Hydroxy-L-tyrosine, a hydroxyl compound of tyrosine.

References:

11. Yang Yan. Pharmacological effects and adverse reactions of dopamine drugs in Parkinson's disease. China Health & Nutrition, 2016.10 (2): 291.
http://med.wanfangdata.com.cn/Paper/Detail/PeriodicalPaper_zgbjyy-kp201627477

7.1.4 Amino acid drugs and nutrients are mainly used to treat depression, polio, tuberculous encephalitis and hyperthyroidism. For example, tyrosine nutrition medicine, tyrosine injection and tyrosine oral liquid, etc.

References:

12. Hu Guangcai. Tyrosine treatment of depression. Medicine and Health Technology. 1981, 2, 36.
https://kns.cnki.net/kcms/detail/detail.aspx?dbcode=CJFD&dbname=CJFD7984&filename=GWYJ198102036&v=pmGXInTBJVhOeSJwK1sfTrDBrs0OHCe5slgLOLcogUv7KjP8pUm4KCnQpE2GeEbr

7.1.5 Some drugs used to treat black aciduria and tyrosinemia, such as nitisinone.

References:

13. Wu Shengnan, Han Lianshu. Progress in diagnosis and treatment of tyrosinemia type I. International Journal of Pediatrics, 2012, 39(4): 393-395.
https://xueshu.baidu.com/usercenter/paper/show?paperid=5d394009912434115a181cb2e5c26990&site=xueshu_se

7.1.6 Some peptide hormones, antibiotics, L-dopa and other drugs, tyrosine is the main raw material for the synthesis of these drugs.

Reference:

http://www.a-hospital.com/w/%E9%85%AA%E6%B0%A8%E9%85%B8

https://www.yixue.com/%E9%85%AA%E6%B0%A8%E9%85%B8

https://www.chemicalbook.com/ProductChemicalPropertiesCB1269334.htm

7.2 Interfering drugs that may cause false negative test results:
If the patient takes certain drugs that cause changes in the body's metabolism, it may cause false negative test results, such as tyrosine inhibitors, traditional Chinese medicines, salicylic acid drugs, vitamin C nutrients and drugs, as well as some sedatives, analgesics, and antihypertensive drugs. Compressive drugs, etc., specifically:

7.2.1Some drugs for the treatment of various tumors and drugs for the treatment of melanin, such as: Lapatinib, vandetanib, Afatinib BIBW-299, cediranib, canertinib, Neratinib HKI-272, bosutinib, Dovitinib, OSI-930, Pelitinib EKB-569, sunitinib, SU6668, motesanib, midostaurin, axitinib, BMS-599626, pazopanib, imatinib, Bafetinib INNO-406, dasatinib, AEE78, vataranib, tratinib, sorafenib (sorafenib), KRN951, CP-547632, gefitinib, erlotinib, nilotinib, Tandutinib MLN518, Fostamatinib R788, ENMD-981693, BIBF1120, Linifanib ABT-869, Ponatinib AP24534, Roxolitinib INCB018424, Aritinib, Apatinib, Icotinib and other drugs are all tyrosinase inhibitors.

References:
14. Liu Jing, Wang Lin, Yang Xiaoming. Research progress of multi-target protein tyrosine kinase inhibitors. International Journal of Pharmaceutical Research, 2009, 36(3):161-171.
https://wenku.baidu.com/view/621ef66b842458fb770bf78a6529647d272834be.html

15. Li Xin, Gao Jinheng, Chen Guoliang. Research progress of protein tyrosine kinase inhibitors. Journal of Shenyang Pharmaceutical University, 2011, 28(2), 1005-1012.
https://www.cnki.com.cn/Article/CJFDTotal-SYYD201112018.htm

7.2.2 Some Chinese medicines have inhibitory effects on tyrosine, including: White peony root, Rhizoma Dioscoreae, Ganoderma lucidum, Peach kernel, Cangzhu, Xinyi, Fatty Sea, Epimedium, Polygonatum, Coix Seed, Polygonum cuspidatum, Platycodon grandiflorum, Schisandra, Yao pollen, Imperata cylindrica, Polygonatum odoratum, Angelica, Rehmannia glutinosa, Aloe, etc.

References:
16. Liu Xinping, Kuang Zhenzhu, Wang Liebing. Discussion on the inhibitory effects of 20 kinds of traditional Chinese medicines on tyrosinase. Seeking Medical Consultation, 2012, 10(8): 75.
https://xueshu.baidu.com/usercenter/paper/show?paperid=c92fa397116a43faa0509f0bb8ad846d&site=xueshu_se

7.2.3 Some salicylic acid drugs have an inhibitory effect on tyrosine in the body, such as acetylsalicylic acid and aspirin.

References:
17. Qian Guoying, Wang Zhijiang, Yin Shangjun, etc. The application of acetylsalicylic acid as a tyrosinase inhibitor. Invention Patent: CN 102871851 A
https://xueshu.baidu.com/usercenter/paper/show?paperid=e841e3f6b88bf0c8288b68ededf2a130&site=xueshu_se

18. Tang Lingzhen, Jianzhe, Liu Bangmin, etc. The effect of aspirin on melanogenesis of normal human epidermal melanocyte line PIG1 cells. Chinese Aesthetic Medicine, 2012, 21(4): 593-595.
https://xueshu.baidu.com/usercenter/paper/show?paperid=e49126b65d0b4521e4406bab6b38ae5d

7.2.4 Some drugs used to treat melasma, such as tranexamic acid, suppress the metabolism of tyrosine.

References:
19. Yang Xihui, Wei Xuling, Li Wen, etc. Clinical and experimental research on the effect of tranexamic acid on tyrosine metabolism. Chinese Journal of Medical Aesthetics, 1998, 4(2): 71-75.
https://xueshu.baidu.com/usercenter/paper/show?paperid=6c1f20e7a357105543fa6ae36aeda379&site=xueshu_se&hitarticle=1

7.2.5 Some drugs may reduce the concentration of tyrosine in the body, such as sedatives, analgesics, antihypertensive drugs, and nutrients and drugs rich in vitamin C.

References:
20. Miao Xiaoqin, Jin Shu. Study on the performance of 3-O-ethyl vitamin C in inhibiting tyrosinase. Daily Chemical Industry, 2009, 39(5): 332-334.
https://xueshu.baidu.com/usercenter/paper/show?paperid=fc02acb55a7734ffcb099dbf83c216ec&site=xueshu_se&hitarticle=1

7.3. Interference factors of diet:
In order to avoid false positive and false negative test results, it is recommended that within 48 hours before the test, the subject should control their diet and consume less health products and high-protein foods. Foods that can increase the content of tyrosine in the body are: Cheese, chocolate and citrous fruit, pickled sardines, tomatoes, milk, lactic acid drinks, cheese, animal liver, beef, yogurt, condensed milk, sausage, ham, fermented food, broad beans, lentils, Pineapple, bananas, figs, tea (various beverages and foods containing caffeine), white wine, fruit wine, beer, vinegar, miso, fermented bean curd, stinky tofu, pine egg, pickled products (such as sauerkraut, kimchi, etc.), mackerel Spanish mackerel, blue ginseng, horse mackerel, tuna, hairtail, sea bass, mullet, yellow croaker, mackerel, carp, oyster, crab, abalone, etc.

Reference:
https://www.360kad.com/medication/596124.shtml

http://www.a-hospital.com/w/%E9%85%AA%E6%B0%A8%E9%85%B8

https://www.yixue.com/%E9%85%AA%E6%B0%A8%E9%85%B8

7.4 Human body's own interference factors:
In the first three days of the test, pay attention to maintaining adequate sleep time, do not stay up late at night, do not participate in strenuous exercise, and avoid extreme fatigue that may cause changes in the immune system and produce emergency responses that will affect the test results. Alcohol allergies After drinking or other allergic reactions are in an allergic state; when the body is in intense exercise, or accompanied by trauma, hypoxia, bleeding, etc., the body will produce a stress response, and the level of adrenaline will increase sharply, speeding up catecholamines and catecholamines. The metabolism of the precursor tyrosine results in a large number of phenolic nucleus compounds in the urine, which may lead to false positive test results.

Rehydration, excessive drinking, and some cancer patients under treatment will have false negative reactions. Patients with advanced cancer often have false negative reactions due to lack of stress response.

Reference:
https://www.360kad.com/medication/596101.shtml

https://www.360kad.com/medication/596124.shtml

21. Pan Xiangfu, Wang Haiming. Tyrosine, catecholamines and stress. Chinese Public Health, 1998, 14(3): 185-186.
https://xueshu.baidu.com/usercenter/paper/show?paperid=bdeb86d84be899fb0fbfac2c5ec0f502&site=xueshu_se&hitarticle=1

22. Pan Xiangfu, Yu Binjiong, Zhang Lin. The mechanism of stress affecting the metabolism of tyrosine and catecholamines. Naval Medicine, 1997, 15(2): 174-177.
https://xueshu.baidu.com/usercenter/paper/show?paperid=cc2fe56376fe19592e6de7b13abc200f&site=xueshu_se&hitarticle=1

7.5 Interfering factors of physical diseases:
Any factors that cause changes in urine color will directly affect the test results, such as: Red urine is also called hematuria. There are many causes of hematuria, the most common are urogenital diseases, such as urinary stones, inflammation, glomerulonephritis, urinary system tumors, and kidney, ureter, bladder and other diseases. In addition, gentamicin and certain sulfa drugs can cause kidney damage and hematuria. Certain drugs, such as rhubarb, the user's urine contains rhein, which is purple-red in the urine.
Yellow urine is common in diseases of the hepatobiliary system, such as acute hepatitis, cholecystitis, and cholelithiasis; common bile duct stones and obstructive jaundice caused by cancer of the head of the pancreas. Drug-induced yellow urine can be seen after taking Adiping and taking vitamin B2 or compound vitamin B tablets will also make the urine dark yellow. Furan antibiotics used to treat urinary tract infections, etc. Its brown metabolites can make urine appear dark yellow. Senna, a traditional Chinese medicine, can also make urine yellow.
Blue urine can be seen in patients with cholera and typhus. Triamterene is a diuretic, and most people can make their urine light blue after taking the drug.
White urine is caused by congenital factors (congenital lymphatic valve dysfunction) and secondary factors (more common in filariasis, abdominal wall tuberculosis, abdominal tumors, chest and abdomen trauma, inflammation, etc.). Also seen in purulent infections of the urinary system, gonorrhea and so on.
Black urine is common in blood transfusions with incompatible blood types, fava bean disease, and falciparum malaria complicated by black urine fever. In addition, taking levodopa and other drugs can also make urine brown.

References:
23. Chen Xiaofeng. Urine color suggests disease. Medicine and Health Care, 2008, 1(1): 111.
https://xueshu.baidu.com/usercenter/paper/show?paperid=f5c09b43c16113efe0cfa06f28176a37&site=xueshu_se

Patients with gastritis and gastric ulcer patients with Helicobacter pylori infection, as well as patients with diabetes are not suitable for the detection of this method. The high level of tyrosine in the body is highly interfering and is prone to false positive results. Patients with Helicobacter pylori infection should be tested after killing Helicobacter pylori in the body.

References:
24. Zhang Huijuan, Liu Xiaomin, Du Baiyan, etc. The relationship between nitrotyrosine level and age, body mass index and other related factors in diabetic patients. China Clinical Rehabilitation, 2004, 10(36): 92-94.
https://www.xueshu.com/zgzzgcyj/200636/26655270.html

7.6 Diseases associated with abnormal tyrosine metabolism:

7.6.1 Parkinson's disease:

Tyrosine can generate dopa in the adrenal medulla and nerve tissue under the action of tyrosine hydroxylase, and then decarboxylate to generate dopamine. After hydroxylation to generate norepinephrine, and then through methylation to generate epinephrine, it becomes Neurotransmitter or hormone, decreased dopamine production in brain tissue can lead to Parkinson's disease.

References:
25. Peng Xiangmin, Jiang Yuping. Tyrosine hydroxylase and Parkinson's disease. Chinese Clinical Neuroscience, 2OO2, 10(1): 105-108.
https://d.wanfangdata.com.cn/periodical/zglcsjkx200201041

26. Zhang Xiaolu, Zhang Fengchun, Li Yaohua. Research on the relationship between tyrosine hydroxylase and Parkinson's disease. Journal of Beihua University (Natural Science Edition), 2005, 6(3): 224-227.
https://d.wanfangdata.com.cn/periodical/ChlQZXJpb2RpY2FsQ0hJTmV3UzIwMjEwNjE2Eg9iaGR4eGIyMDA1MDMwMDkaCGY5dWNsemFy

7.6.2 Mild depression:

Tyrosine is the precursor of neurotransmitters—norepinephrine and dopamine, which can regulate mood and perform other functions. Tyrosine is an emotional stimulant. Lack of enough tyrosine can cause a lack of norepinephrine in the brain, causing some mood disorders, such as mild depression.

References:
27. Wu, Kaida Jiang, Jianying Qiu et al. Association analysis of tyrosine kinase receptor B gene polymorphism and depression. Journal of Shanghai Jiaotong University (Medical Edition), 2010, 30(6): 620-623.
https://d.wanfangdata.com.cn/periodical/ChlQZXJpb2RpY2FsQ0hJTmV3UzIwMjEwNjE2EhNzaGRleWtkeHhiMjAxMDA2MDA0Gghkd25qZm01eA%3D%3D

7.6.3 Albinism:

Tyrosine is catalyzed by tyrosinase to produce dopa in melanocytes, and then through oxidation, decarboxylation, and other reactions, melanin is finally produced. Congenital deficiency of tyrosinase causes albinism.

Albinism is a hereditary leukoplakia caused by a lack of melanin in the skin and accessory organs or a synthesis disorder caused by tyrosinase deficiency or hypofunction. The disease is a family hereditary disease, which is mainly inherited in an autosomal recessive manner. The main clinical manifestations are the lack or reduction of melanin in the skin, hair and eyes of the whole body, the skin and body hair are white or yellow-white, the retina is not pigmented, and the iris and pupil are pale pink and photophobia. According to the different tissues invaded, albinism can be divided into oculocutaneous albinism (OCA), whose lesions are limited to the skin and eyes, and ocular albinism (OA), whose lesions are limited to the eyes. The incidence of albinism in the population is about 5 to 10 per 100,000. It can occur in all races without gender differences, and it is more likely to occur in people who are married to close relatives.
Tyrosinase can convert tyrosine into melanin. Type I patients have mutations in the tyrosinase gene that cause lack of tyrosinase activity (type IA), decreased activity (type IB, I-MP), or lower enzyme activity. Decreased at higher temperatures (I-TS type), tyrosinase is a key enzyme in the melanin biosynthesis pathway, and its lack or decrease in activity can lead to reduction or loss of skin pigmentation. Type II patients have P gene deletion or mutation, resulting in loss of P protein function. P protein is related to the transport of melanin precursor tyrosine into the melanosome membrane and is a protein necessary for the production of melanin. Loss of P protein function can lead to Melanin synthesis disorder. Type III patients are mainly caused by mutations in the gene encoding tyrosine-related protein 1 (TYRP1).

Reference:

https://www.yixue.com/%E7%99%BD%E5%8C%96%E7%97%85

28. Zhang Zhongshou. Related research on genetic genes of various types of ocular skin albinism. China Medical Herald, 2011, 8(25): 155-156.
https://d.wanfangdata.com.cn/periodical/ChlQZXJpb2RpY2FsQ0hJTmV3UzIwMjEwNjE2Eg95eWN5engyMDExMjUwNzMaCGF1Z2dmZTg5

29. Peng Chen, Deng Weiping. Research progress in albinism. International Journal of Dermatology and Venereology. 2014, 40(1): 26-28.
https://d.wanfangdata.com.cn/periodical/ChlQZXJpb2RpY2FsQ0hJTmV3UzIwMjEwNjE2EhNnd3l4LXBmeGJ4MjAxNDAxMDEwGghncHppMTllcw%3D%3D

7.6.4 Pigment disorders (freckles, brown spots) and malignant melanoma:
Tyrosinase (EC 1.14.18.1) is a copper-containing oxidoreductase, which is widely present in animals, plants and microorganisms, and is directly related to the synthesis of pigments in organisms. In the human body, it is associated with pigment disorders and malignant diseases. The occurrence of melanoma tumors is related to treatment.
Tyrosinase is mainly involved in two reaction processes: it catalyzes the hydroxylation of L 2 tyrosine into L 2 dopa and oxidizes L 2 dopa to form dopaquinone. After a series of reactions, dopaquinone forms melanin. Tyrosine Acid enzyme has an important physiological function in the organism. At the same time, it is also related to the occurrence of diseases such as excessive deposition of melanin such as freckles and brown spots in the human body.

References:
30. Chen Qingxi, Song Kangkang. Research Progress in Tyrosinase. Journal of Xiamen University (Natural Science Edition) 2006, 45(5): 731-737.
https://d.wanfangdata.com.cn/periodical/ChlQZXJpb2RpY2FsQ0hJTmV3UzIwMjEwNjE2Eg94bWR4eGIyMDA2MDUwMzMaCGgxaWF2aGpm

7.6.5 Black aciduria and phenylketonuria:
Tyrosine can also be catalyzed by transaminase to produce p-hydroxyphenylpyruvate, which is transformed into fumaric acid and acetoacetic acid through intermediate products such as homogentisic acid. Therefore, phenylalanine and tyrosine are sugar-producing and ketogenic amino acids. Homogenic acid catabolism enzymes are congenital defects, and homogentisic aciduria can occur.
In the absence of phenylalanine hydroxylase, phenylalanine cannot be converted into tyrosine, phenylalanine accumulates, and a large amount of phenylpyruvate is generated by transamination, which is further converted into phenylacetic acid. At this time, a large amount of metabolites such as phenylpyruvate appear in the urine, which is called phenylketonuria.

References:
31. Ma Jingran, Qiu Zhengqing. Clinical analysis of a case of black aciduria caused by HGD gene mutation. 2015 Annual Meeting of Pediatrics Branch of Beijing Medical Association.
https://xueshu.baidu.com/usercenter/paper/show?paperid=1f1x0rw0ak3w0m70kj700230eb346580&site=xueshu_se

32. Zhang Zhi, He Yunshao. Progress in molecular genetics of phenylketonuria. Heredity, 2004, 26 (5): 729-734.
https://d.wanfangdata.com.cn/periodical/ChlQZXJpb2RpY2FsQ0hJTmV3UzIwMjEwNjE2Egt5YzIwMDQwNTAzMRoIb2QxNHZqN2s%3D

7.6.6 Tyrosinemia:
Tyrosinemia is a rare autosomal recessive genetic metabolic disease. Due to tyrosine degradation, damage to multiple organs such as brain, liver, kidney, bones, etc., has a poor prognosis and a high rate of death and disability. Different types of patients have different clinical manifestations. Low-tyrosine diet and drug therapy are the main intervention methods, and liver transplantation is necessary if necessary.
According to different defective enzymes, tyrosinemia is divided into three types:
1. Tyrosinemia type I is due to FAH gene mutations leading to defects in the terminal enzyme fumaryl acetoacetate hydrolase in the tyrosine metabolism process, tyrosine and its metabolites succinylacetone, 4-hydroxyphenyllactic acid and 4 -Accumulation of hydroxyphenylpyruvate, etc.
2. Tyrosinemia type Ⅱ is caused by tyrosine aminotransferase deficiency.
3. Tyrosinemia type III is a disease caused by a deficiency of 4-hydroxyphenylpyruvate dioxide.
Clinical manifestations:
The condition of patients is different, and there are significant individual differences. Most untreated patients die before the age of 10, and the prognosis of early detection and treatment can be greatly improved.
1. Tyrosinemia type I
According to the age of onset, it is divided into acute type, subacute type and chronic type.
(1) Acute type

The child develops symptoms within a few days to a few weeks after birth. The main clinical manifestations are acute liver failure, jaundice, anorexia, bleeding tendency, vomiting, pale skin, slow growth, hepatomegaly, and rapid progress of the disease. If not treated, Most die within 1 year of age.
(2) Subacute and chronic types
The onset usually occurs between 6 months and 2 years of age, liver, kidney, and nerve damage. Some children have rickets, reflexes, etc., and the children often cry because of severe pain. If untreated, it can develop into hepatocellular carcinoma.
2. Tyrosinemia type II
The child is mainly characterized by ocular symptoms. A few months after birth, symptoms such as tearing, photophobia, and conjunctival congestion appear, followed by corneal ulcers and opacity, nystagmus, etc., and blisters, ulcers and hyperkeratosis on the palms and soles of the hands. Intellectual and developmental disabilities after age.
3. Tyrosinemia type III
Children are generally asymptomatic. Mild mental retardation, cramps, and ataxia may also occur.

References:
13. Wu Shengnan, Han Lianshu. Progress in diagnosis and treatment of tyrosinemia type I. International Journal of Pediatrics, 2012, 39(4): 393-395.
https://xueshu.baidu.com/usercenter/paper/show?paperid=5d394009912434115a181cb2e5c26990&site=xueshu_se

33. Han Lianshu, Ye Jun, Qiu Wenjuan, etc. The application of succinylacetone detection in blood and urine in the diagnosis of tyrosinemia type I. Chinese Journal of Pediatrics, 2012, 50(2): 126-130.
https://d.wanfangdata.com.cn/periodical/ChlQZXJpb2RpY2FsQ0hJTmV3UzIwMjEwNjE2Eg16aGVrMjAxMjAyMDEwGghsMmx5aXBhcA%3D%3D

7.6.7 Malignant tumors:
Mainly include gastrointestinal malignancies (gastric cancer, bowel cancer), liver cancer, nasopharyngeal cancer, lymphoma, breast cancer, gynecological malignancies, lung cancer, etc. Increased level of monohydroxyphenol metabolites (tyrosine) in urine is mainly related with the detection of abnormal amino acid metabolism in patients with malignant tumors, and it has appeared in the early stage of tumor. At this time, protein decomposition is enhanced, and amino acid catabolism is weakened. Amino acids are reused in tumor cell protein synthesis, and excess unusable amino acids are excreted.
A large number of experimental studies have found that the tyrosine content in the urine of almost all patients with malignant tumors increases significantly, reaching 50% to 150%, far exceeding level by normal health people. The positive detection rate of urine tyrosine in patients with malignant tumors is significantly higher than that of normal health people and patients with benign tumors. The difference is statistically significant for different types of malignant tumors such as gastrointestinal malignancies (gastric cancer, bowel cancer), liver cancer, nasopharyngeal cancer, lymphoma, breast cancer, gynecological malignant tumors, lung cancer, etc.
When the level of monohydroxyphenol metabolites (tyrosine) in urine is higher than average, it only indicates that there is abnormal tyrosine metabolism in the human body, and it cannot diagnose malignant tumors. It needs to be combined with other detection methods to exclude and diagnose. However, because of the above-mentioned characteristics, it can be used as a means of early tumor screening in clinical practice, and it has more important significance for the early diagnosis of tumors.

References:
34. Luo Yang, Wang Jue, Zhang Xue, etc. The application of the detection of amino acid metabolites in urine in the screening of malignant tumors. Journal of Modern Laboratory Medicine, 2009, 24(2): 66-69.
https://d.wanfangdata.com.cn/periodical/ChlQZXJpb2RpY2FsQ0hJTmV3UzIwMjEwNjE2Eg9zeHl4ankyMDA5MDIwMTcaCDI0b3hpcTJr

35. Huang Xuemei, Wu Lixiang, Lu Zilan, etc. The application value of urine p-hydroxyphenylalanine in the early prediction of malignant tumors. Laboratory Medicine and Clinics, 2015, 12(16): 2333-2335.
https://d.wanfangdata.com.cn/periodical/ChlQZXJpb2RpY2FsQ0hJTmV3UzIwMjEwNjE2EhBqeXl4eWxjMjAxNTE2MDE0GghpdjR1ZXQ3Ng%3D%3D

36. Fan Yang, Jingjing Li, Haijun Deng et al., GSTZ1-1 Deficiency Activates NRF2/IGF1R Axis in HCC via Accumulation of Oncometabolite Succinylacetone, EMBO J (2019)38:e101964.
https://www.embopress.org/doi/full/10.15252/embj.2019101964

37. Xiang Daijun, Wang Chengbin, Wang Hai. Value of quick detection for urine monohydroxyphenyl metabolite in diagnosing malignant tumor. Lab Med Clin, March 2016, Vol13, No.6
https://www.docin.com/p-1782985206.html

38. Li Fusen, Hou Huaxin, Zhao Nong, Liang Yonghong, Huang Yanjun. Clinical Significance of Determination of Monohydric Phenols in Urine in Diagnosis of Nasopharyngeal Carcinoma. Cancer research and clinic, 2008, 12(4).
https://kns.cnki.net/kcms/detail/detail.aspx?dbcode=CJFD&dbname=CJFD2000&filename=ZLYJ200004013&uniplatform=NZKPT&v=Uc1eB4SpdkiHCAarQC0SdKRCdDDqFP6nT7q7GuNa6mn-Tpj_hkKCL37MfgmfaFFn

39. Hou Huaxin, Zhao Nong, Liang Yonghong, Huang Yanjun, Li Rongdan. Clinical Significance of Determination of Monohydroxyphenols in Urine for Diagnosis of Gynecological Tumors. Cancer prevention research, 1999 (6), 412-413.
https://kns.cnki.net/kcms/detail/detail.aspx?dbcode=CJFD&dbname=CJFD9899&filename=ZLFY199906004&uniplatform=NZKPT&v=J0J3nyKyDrIs_k9eAoChpMx9iUPPmJaops6qVOwUVbclpTNAasVHmesczwj5mRC

40. Zhao Yajing, Jia Wenyu. Clinical Significance of Determination of Urinary Monohydric Phenol Derivatives in the Diagnosis of Malignant Tumors. Journal of Modern Integrative Medicine. 2000, (11). 1031.
https://kns.cnki.net/kcms/detail/detail.aspx?dbcode=CJFD&dbname=CJFD2000&filename=XDJH200011047&uniplatform=NZKPT&v=QxlpDARSklzktnE0EZIH6AABNRCoNEkIhuRX_QhY1GB76DLDndfomC5mKNNnqk-

41. Song Hui, Hou Huaxin, Li Fusen, Huang Yanjun, Liang Yonghong, Zhao Nong. Study on the determination method of monohydric phenols in urine and its application in tumor screening. Chinese Journal of Modern Medicine. 2003, (02). 71-72.
https://kns.cnki.net/kcms/detail/detail.aspx?dbcode=CJFD&dbname=CJFD2003&filename=ZXDY200302030&uniplatform=NZKPT&v=jwTL3YvxH344uyQROE54pfUA6FfscRYWNiIBbIvhWpu4Nl5Xbevsg0pIK529JVr9

8. Literature research conclusion

According to the above literature review, factors that may cause tyrosine content changes in urine are food or drugs that can decompose and activate a large amount of amino acids; certain drugs that inhibit the breakdown of amino acids; patients with gastritis and gastric ulcers who are accompanied by Helicobacter pylori infection, as well as patients with diabetes; people's physical condition. Factors that can cause changes in urine color include: red urine, dark yellow urine, blue urine, and black urine. We also can state that low level or high level of monohydroxyphenol metabolites (tyrosine) in urine points out on different types of diseases. But high level is mainly correlated with malignant tumors and other cancer diseases.

9. User manual recommendation

Interference factors and precautions that may occur during the use of this reagent include:
Interference factors that may cause false positive test results:
After the tester eats food or drugs that can decompose and activate a large amount of amino acids, the test result may be false positive. For example, peptide and hormone drugs, traditional Chinese medicine, central nervous system drugs, amino acid drugs, and tyrosine-rich health products and high-protein foods.
Interference factors that may cause false negative test results:
After taking certain drugs that inhibit the breakdown of amino acids, the tester's reduced metabolites in the urine can lead to false negative test results. For example, tyrosine inhibitory drugs, traditional Chinese medicine, salicylic acid drugs, vitamin C nutrients and drugs, as well as some sedative, analgesic, and antihypertensive drugs.
Other interference factors that are not suitable for this test:
When using this reagent for testing, it is required that the tested specimen is a fresh and clean urine sample, and the urine color changes abnormally due to physical diseases, such as red urine, dark yellow urine, blue urine, black urine, etc., which is not suitable for this item detection.
When using this reagent for testing, the subject is required to maintain a good physical condition. It is not suitable for physical conditions such as extreme fatigue, allergies, intense exercise, trauma, hypoxia, bleeding, fluid replacement, excessive drinking, etc. Item detection.
When this reagent is used for testing, patients with gastritis and gastric ulcers who are accompanied by Helicobacter pylori infection, as well as patients with diabetes, are not suitable for this test.
Precautions when using this reagent for testing:
It is recommended that the tester get enough sleep and use morning urine before being tested. As for the drugs that may affect, tester need to consult the doctor for confirmation. This can avoid false positive and false negative results to a large extent, and further improve the accuracy of he test results.

10, References and list of documents

References have been made in each of the above sections.