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蓝藻毒素对底栖动物的毒理学研究进展

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摘要:近年,由于人类活动加剧,大量氮磷等营养物质流入湖泊等缓流水体,导致水体富营养化。而由此引起有害蓝藻水华的频繁爆发,使生态环境和人类健康受到严重威胁。相关研究表明,蓝藻水华的爆发不仅能够使水体水质恶化,其中一些产毒藻类还会产生大量蓝藻毒素,对水生生物产生重要影响。底栖动物作为水体生态系统的重要组成部分,在食物网中有重要作用,同时其中的许多种类又与人类息息相关,因此关于水华蓝藻毒素对淡水底栖动物的毒理学研究具有重要意义。在介绍蓝藻毒素概况的基础上,综述了蓝藻毒素的致毒机理和对底栖动物的影响,展望了研究方向。

关键词:底栖动物; 蓝藻毒素; 食物网; 环境毒理学

Advances on cyanotoxin toxicology of zoobenthos

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Abstract: In recent years, owing to the intensified human activities, a large number of nutrients, primarily nitrogen and phosphorus, flow into lakes and other water bodies and result in serious eutrophication. However, the cultural eutrophication is often associated with cyanobacteria blooms which can create significant water quality and human health problems. What's more, some species of cyanobacteria are capable of producing secondary metabolites named cyanotoxins. Mass populations of toxin-producing cyanobacteria are in natural and controlled water bodies include blooms and scums of planktonic species, and mats and biofilms of benthic species. Toxic cyanobacterial populations have been reported in freshwaters in over 45 countries. These toxins can be classified into five main types according to their mechanism of action in vertebrates: hepatotoxins, cytotoxins, dermatotoxins, neurotoxins and irritant toxins. These toxins (microcystins, nodularins, saxitoxins, anatoxin-a, anatoxin-a(s), cylindrospermopsin) are structurally diverse and their effects range from liver damage, including liver cancer, to neurotoxicity. There are more than 80 microcystin congeners, microcystin-LR (L, L-leucine; R, L-arginine) is the best studied cyanobacterial toxin, whereas information for the other toxins is largely lacking. Many studies on the effects of cyanobacteria and their toxins over a wide range of aquatic organisms, including invertebrates and vertebrates, have reported acute effects (e.g., reduction in survivorship, feeding inhibition, paralysis), chronic effects (e.g., reduction in growth and fecundity), biochemical alterations (e.g., activity of phosphatases, GST, AChE, proteases), and behavioral alterations. Research has also focused on the potential for bioaccumulation and transferring of these toxins through the food chain. In general, the toxins can transfer to human bodies by drinking and very little by entertainment or health care products. In some special circumstances, the toxins can also be transferred into human

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bodies by dialysis. Be the highest level of the food chain, toxins can also transfer to human beings by eating aquatic products. As an important part of the aquatic ecosystem, zoobenthos plays an important role in the aquatic food web. On the one hand, it plays an important part in the material and energy flow process. It is not only the source of the predacity fish, but also the predator of the phytoplankton, zooplankton or organic detritus. On the other hand, some species of the zoobenthos can also be used in water cleaning and influence the formation of the eutrophication. The most important thing is that many of them are even closely related to human beings (directly or indirectly food sources), especially the people leave around the lakes and other water bodies, so the study of the cyanotoxin toxicology of zoobenthos is of great importance. In this review, we first summarized the mechanism of toxicity of cyanotoxin on zoobenthos on the base of a brief introduction of cyanotoxins, with emphasis on microcystins. Secondly, the effects of cyanotoxins on zoobenthos is discussed in details, including the bioaccumulation and elimination of the cyanotoxin, the effects of cyanotoxin and the food web studies about cyanotoxin (mainly microcystis) in zoobenthos. At last, we prospect the further research directions as well as drawbacks and future needs in this field of research.

Key Words: zoobenthos; cyanotoxin; food web; environmental toxicology

由于人类活动的加剧,氮磷等植物营养物质大量流入水体,造成水体富营养化,在与光照、温度、浊度、pH 值、电导率、盐度和一些水文条件(如水体的流动性)等相互影响后[1],最终使一些光能自养型藻类大量繁殖而导致藻类水华爆发。淡水水体水华的发生主要以蓝藻水华为主,蓝藻的大量繁殖不但会对水体造成直接影响(如溶解氧降低等),还能够产生毒性很强的代谢产物——蓝藻毒素(cyanotoxin),危及动物和人类安全。

底栖动物是水体中与蓝藻毒素具有最直接关系的一类水生生物。底栖动物是指生活史的全部或大部分时间生活于水体底部的水生动物类群,是水生态系统的一个重要组成部分[2]。底栖动物在水生态系统中发挥着重要作用。首先,它们可以加速水底物质分解,促进水体自净;其次,底栖动物是水体生态系统食物链的重要组成部分,不仅是浮游生物的捕食者,还是一些掠食动物(Predators)的食物,有的杂食种类还能充当分解者;再次,底栖动物在水体富营养化研究中有重要作用,它们可以通过自身的生命活动对水体中营养盐的含量产生重要影响,其中的一些物种已经被用于水体富营养化的治理。同时,底栖动物中有许多物种不仅是一些水产品的重要饵料,还是倍受人类欢迎的美食。所以,研究蓝藻毒素对底栖动物的毒理学具有重要的理论和实际意义。有鉴于此,本文综述了蓝藻毒素对底栖动物的毒理学研究现状,对蓝藻毒素的基本性质、致毒机理、在生物体内的累积与清除,以及对底栖动物的影响进行了综述,并进一步对未来研究重点进行了展望,以期能够为今后对蓝藻毒素的进一步研究提供参考。

1 蓝藻毒素概述

自 1878 年首次报道蓝藻毒素导致家禽死亡后,世界范围内关于蓝藻毒素对动物和人类危害的报道越来越多,当家畜及野生动物饮用含有藻毒素的水之后,一般会出现肝脏肿大、充血或坏死,肠炎出血、肺水肿等病变,同时因接触蓝藻毒素而导致的人类死亡事件也时有发生,而有学者亦指出中国南方原发性肝癌的高发病率与饮用水中含有微囊藻毒素(Microcystin, MC)存在一定的关系[3-6]。相关研究发现,蓝藻毒素为蓝藻的次级代谢产物,在不同生境都有广泛的分布[7]。蓝藻毒素根据化学结构可以分为三类:环肽(Cyclic peptide)、生物碱(Alkaloid)和脂多糖内毒素(Lipopolysacchride, LPS);也可根据毒素作用位置的不同分为肝毒素(Hepatotoxin)、神经毒素(neurotoxin)、细胞毒素(cytotoxin)和皮肤毒素(dermatotoxin)等[8]。而其中微囊藻毒素(MC)是世界各地最为常见且危害最严重的毒素,具有显著的肝脏毒性,其结构在 20 世纪 80 年代初得到确认,为环状七肽结构,目前已发现 80 余种毒素亚型,最常见的为 MC-LR,在世界范围内得到最广泛的关注[9-11]。除 MC 之外,对其它毒素(如节球藻毒素(Nodularin)、拟柱孢藻毒素(Cylindrospermopsin,CYN)和生物碱毒素等)的研究相对较少。

相关研究发现,MC 的性质稳定,大多数 MC 是亲水的,一般在水中的溶解度能达到 1 g/L 以上,不易沉淀或被沉积物和悬浮颗粒物吸附,易溶于甲醇或丙酮。由于 MC 分子结构中含有羧基、氨基和酰氨基,所以在不同 pH 值条件下 MC 有不同的离子化倾向[12],但蛋白质水解酶对它们却不起作用。MC 还具有热稳定性,在加热到 300 ℃后仍能维持很长时间不分解[1]。MC 在阳光照射下亦非常稳定,但是在不同浓度的水可提取色素存在的条件下它的稳定性和异构化有显著的变化[8],同时在某些条件下 MC 能够被生物所降解。

2 致毒机理

由于 MC 具有亲水性导致其不能以被动运输的方式通过细胞膜,而只能依靠相应载体的运输,这也是 MC 器官选择性毒性的重要原因[13],MC 在动物细胞中的迁移转化过程如图 1[14] 所示。MC 致毒的分子机制主要有以下几个方面:抑制蛋白磷酸酶的活性、引起氧化应激和内质网应激。研究发现微囊藻毒素和节球藻毒素可以与蛋白磷酸酶(protein phosphatases, PPs)1 和 2A 的丝氨酸/苏氨酸亚基相结合,从而抑制它们的活性[15-17]。由于蛋白磷酸酶在催化蛋白分子脱磷酸化和调控细胞骨架与细胞凋亡等过程中具有重要的作用,所以当蛋白磷酸酶 PP1 和 PP2A 被抑制时,会导致细胞过度磷酸化,甚至使细胞凋亡[18]。同时,蛋白磷酸酶的抑制可使 DNA 依赖的蛋白激酶(DNA-dependent Protein Kinase, DNA-PK)失活,进而造成 DNA 的损伤[19-20]。MC 还能够引起活性氧簇(Reactive oxygen species, ROS)的快速产生,而 ROS 的大量产生会导致脂质过氧化、线粒体结构和功能的破坏和 DNA 损伤等。而 MC 对细胞内抗氧化系统的损伤主要是在与 OATP(Organic anion transporting polypeptides,有机阴离子转运多肽)载体结合进入细胞时谷胱甘肽(Glutathione, GSH)的流出导致的[10,21-23]。目前对于内质网应激的研究还相当少,但已有研究表明,MC 可能导致错误折叠的蛋白质在内质网内堆积,从而引起内质网应激[24]。随着不断的研究发现,MC 的毒性作用在最后几乎都能导致细胞的凋亡,同时还有一定的促癌作用,而对于蓝藻毒素在生物体内的转化还需要进一步深入的研究。

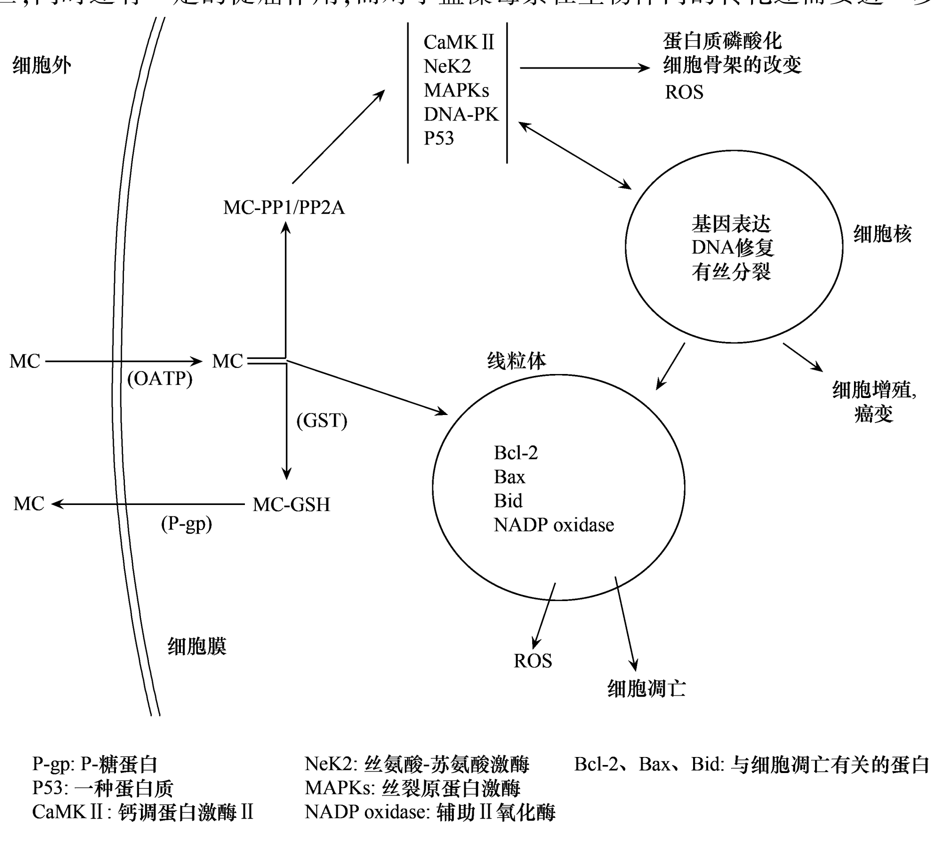

图 1 动物细胞中微囊藻毒素 MC 的摄取、毒性机制、生物转化和排泄的路径[14]

Fig.1 Suggested pathways of MC up-take, toxicity, biotransformation and excretion in animal cells[14]

3　蓝藻毒素与底栖动物

蓝藻毒素对淡水水生生物作用的研究较少且大多集中于一些鱼类和某些大型的底栖动物,原因可能主要有以下几个方面:一方面,与海洋藻毒素相比,淡水藻毒素对人类和一些动物产生的急性中毒事件较少;第二,人类对淡水水产品的消耗量与海洋水产品的消耗量相比要小的多,联合国食品与农业组织调查发现,2008 年全球捕鱼量为 9000 万 t,而内陆淡水捕鱼量只有 1000 万 t[25];第三,所研究的淡水水生生物大都是被人类食用的食物(如螺、蚌和虾等),对人类可能存在较大的潜在危害;同时,研究还会受生物个体特征、实验和检测分析条件的限制,如生物食性、生物量大小、存活能力和体内毒素含量。目前的研究基本集中在生物体内或者不同器官中藻毒素富集和清除的研究,也有一些藻毒素在同一生物不同器官中分布和对不同成长阶段个体影响的研究,但对于藻毒素在生物体内的分子生物学转化及代谢和生物链中转移机制方面的研究则相对较少。

3.1　蓝藻毒素在底栖动物体内的富集与清除

底栖动物通过不同的方式富集 MC 后,MC 大部分富集于消化道、肝胰腺和性腺三个器官之内,以消化道和肝胰腺中的含量最高,多数研究结果都已超过 WHO 的规定(0.04 $\mu g\ kg^{-1}\ d^{-1}$)[26],关于蓝藻毒素在底栖动物体内的富集与清除详见表 1。相对来说,底栖动物的足和肌肉中 MC 的含量要小的多,所以在只食一些底栖动物的足或者肌肉的情况下,MC 对于人类健康的影响相对较小[27-36]。研究表明,MC 在底栖动物体内的富集与一些环境因子存在一定的相关性。如 Ozawa[29] 等研究淡水田螺(*Sinotaia histrica*)肝胰腺和肠道中 MC 的季节变化时发现,当湖泊中浮游植物体内 MC 含量最高时(10 月),田螺肠道和肝胰腺中的 MC 的含量也最高,而 Yokoyama 和 Park[37] 发现褶纹冠蚌(*Cristaria plicata*)在夏季水华时 MC 含量很低,但是在水华消失的秋季却迅速升高;Chen 和 Xie[31] 对 3 种双壳类的研究得出,夏季大部分器官 MC 含量的峰值与悬浮颗粒物和水华蓝藻的 MC 含量峰值相吻合,同时,Chen 和 Xie[33] 还指出不同底栖动物中不同的 MC 含量可能与摄取的食物不同有关。Lance[38] 等和 Prepas[39] 等的研究表明,静水椎实螺(*Lymnaea stagnalis*)和淡水无齿蚌(*Anodonta grandis simpsoniana*)对 MC 的富集主要通过摄食含有毒素的浮游植物,而极少通过吸收溶解的毒素,而 Zhang[40] 等对椭圆萝卜螺(*Radix swinhoei*)和螺狮(*Margarya melanioide*)各器官对 MC 的生物富集的研究却发现,椭圆萝卜螺中 MC 浓度与环境中的溶解 MC 有关,而螺狮中的 MC 浓度与细胞内毒素相关。Zhang[30] 等对太湖中铜锈环棱螺(*Bellamya aeruginosa*)的研究还发现,后代体内 MC 含量还与母体性腺中 MC 的含量有关。Zhang[9] 等对太湖铜锈环棱螺肝胰腺中 3 种最常见的毒素亚型(MC-LR、MC-RR 和 MC-YR)的时空分布的研究指出,MC 在肝胰腺中浓度的变化与不同点位水体中细胞内毒素的变化一致,且与悬浮颗粒物中 MC 浓度显著相关,同时结果表明其它因素(如水温)对铜锈环棱螺肝胰腺内的 MC 富集有重要的影响;当底栖动物处于不同的营养级时,其体内 MC 的含量也会有很大的差别[35]。Galanti[42] 等在室内对淡水虾 *Palaemonetes argentinus* 的研究发现,将 *P. argentinus* 在 MC-LR(50 μg/L)中培养 3 d 后就能检测到 MC,同时还指出 MC 与 GSH 的结合是 *P. argentinus* 的一种重要的 MC 解毒机制。

目前对拟柱孢藻毒素(CYN)等其它毒素生物富集的研究相对较少。Seifert[43] 的研究显示 CYN 在低于 100 μg/L 情况下就能对一些水生无脊椎动物产生显著的影响。Saker 和 Eaglesham[44] 第一次对红螯螯虾(*Cherax quadricarinatus*)肌肉和肝胰脏中 CYN 的浓度进行了检测,发现肝胰腺和肌肉组织中含量分别达到 4.3 和 0.9 mg/kg(干重),而室内研究结果要比野外低很多。Saker[45] 等将淡水无齿蚌(*Anodonta cygnea*)暴露于不同浓度的 CYN 中,发现各器官中所占比例为血淋巴 68.1%,内脏为 23.3%,足和性腺为 7.7%,外套膜 0.9%,在鳃和肌肉中未发现,而且在经过 14 d 的清除之后还有大约 50%的毒素存留。White[46] 等在实验室内对瘤拟黑螺(*Melanoides tuberculata*)的研究发现腹足类亦有富集 CYN 的能力。而 Berry 和 Lind[47] 对一腹足类(*Pomacea patula catemacensis*)的野外研究发现,组织中毒素含量为(3.35±1.90)ng/g,但是生物富集系数却为 157,说明 CYN 浓度非常低时也会发生生物富集。Wood[48] 等对淡水小龙虾(*Paranephrops planifrons*)的研究发现,其肝胰腺中 nodularin-R 浓度(9.7—225.3 μg/kg, 湿重)显著高于尾部组织的浓度(0.5—0.7 μg/kg, 湿

重)。Galanti[42]等将 *P. argentinus* 放入含有节球藻毒素的水库后发现,3 周后 *P. argentinus* 中也能检测到节球藻毒素。Kankaanpää[49]等发现节球藻毒素在海产贻贝、斑纹蚌(*Dreissena polymorpha*)和波罗的海白樱蛤(*Dreissena polymorpha*)中都有富集现象。除以上几种毒素的研究外,还有少量对其它毒素在底栖生物中富集与清除的研究[50-51]。

表 1 蓝藻毒素在底栖动物体内的富集与清除

Table 1 Accumulation and depuration of the cyanotoxins in the zoobenthos

藻及毒素种类 Algae and toxin species	研究地区 Study areas	底栖动物种类 Zoobenthic species	毒素的富集与清除 Toxin accumulation and elimination	文献来源 References
微囊藻属 *Microcystis*,MC	日本 Suwa 湖	淡水田螺	消化道毒素含量最高(9.03 μg/g),可以高效清除 MC-LR	[27]
铜绿微囊藻 *Microcystis aeruginosa*,MC	葡萄牙 Mira 湖	克氏原螯虾	体内最大浓度达 2.9 μg/g,肠道含量最高,清除与一些贝类的研究相似	[28]
鱼腥藻与微囊藻属 *Anabeana* & *Microcystis*,MC	日本 Biwa 湖	淡水田螺	肠道中最高为 19.5 μg/g,富集能力强	[29]
微囊藻属 *Microcystis*, MC	中国太湖 贡湖湾	铜锈环棱螺	肠(53.6%)>肝胰脏(29.9%)	[30]
铜绿微囊藻 *Microcystis aeruginosa*,MC	葡萄牙室内实验	紫贻贝	富集阶段最高为 0.38 μg/g,清除阶段浓度出现升高	[41]
微囊藻属 *Microcystis*, MC	中国太湖	三角帆蚌、褶纹冠蚌和背瘤丽蚌	肠道和肝胰脏中含量最高,褶纹冠蚌肝胰腺中 MC 含量高于其它两种	[31]
铜绿微囊藻 *Microcystis aeruginosa*,MC	巴西,帕图斯泻湖	双壳类(*Mesodesma mactroides*)	肝胰腺中的最大浓度可达(5.27±0.23)μg/g	[32]
微囊藻属 *Microcystis*,MC	中国太湖 梅梁湾	背角无齿蚌、三角帆蚌、褶纹冠蚌、背瘤丽蚌	毒素主要分布在肝胰腺之中(45.5%—55.4%),且不同物种有所不同	[33]
微囊藻属 *Microcystis*,MC	中国巢湖	铜锈环棱螺	肝胰腺(平均 4.14 μg/g)中 MC 含量显著高于消化道或者性腺	[34]
微囊藻属 *Microcystis*,MC	中国巢湖	秀丽白虾和日本沼虾	两种虾器官中平均 MC 含量胃>肝胰腺>性腺>鳃>肌肉,且各器官间含量无相关性	[35]
铜绿微囊藻 *Microcystis aeruginosa*,MC	中国室内试验	三角帆蚌	肝胰腺中 MC-LR 的含量最高((55.78±6.73) μg/g),有较强的抗毒能力,可被用来控制有毒蓝藻水华	[36]

3.2 蓝藻毒素对底栖动物的毒理作用

蓝藻毒素对底栖动物的毒性作用主要有急性毒性,如存活个体的减少、摄食的抑制和麻痹等;慢性毒性,如对生长和繁殖的影响;生物化学的变化,如磷酸酶、谷胱甘肽 S 转移酶和蛋白酶等活性的改变等;还有就是对动物行为的影响[52]。

MC 对腹足类生活史特征的影响因生物年龄、暴露方式(产毒藻类或者溶解性 MC)和是否存在无毒食物的不同而不同,实验研究发现 MC 能够导致胚胎发育变缓,孵化成功率和后代存活率降低[53]。Zhu[54]等用两种暴露方式(单一有毒蓝藻和有毒蓝藻与无毒绿藻混合)对铜锈环棱螺进行处理,然后观察螺肝胰腺超微结构和生物化学反应的变化,发现在中毒阶段后期肝中酸性磷酸酶、碱性磷酸酶和谷胱甘肽 S 转移酶活性显著升高,而在清除阶段酶的活性又回到原来水平,同时出现细胞质严重液泡化、细胞核压缩变形、线粒体膨胀成髓状、内质网粗面被破坏和溶酶体增殖等现象,并观察到细胞凋亡,放到无毒藻类处理中这些现象便消失,这些反应可能是细胞用来减少伤害的适应机制。这与 Martins[55]等对 MC 与底栖动物相互作用所表现出得生物化学反应的研究结果相似。Puerto[56]等对拟柱孢藻毒素对两种双壳类细胞内生物化学反应的影响进行了研究。毒素对生物的胚胎发育也有负面的影响,而且能够从受污染的母体性腺中传递到后代体内[33,57]。Lance[58]等对淡水螺(*Potamopyrgus antipodarum*)的研究就发现,MC 不仅能够影响螺的生存和生长,而且对它的繁殖也产生了一定影响。MC 对不同底栖动物的群落结构也会产生显著的影响,Lance[53]等发现腹足类前

鳃亚纲和肺螺亚纲种群对 MC 有不同的反应,而肺螺亚纲对 MC 的抗性更强;Gérard[59]等的研究指出在受 MC 严重污染的水体中软体动物丰度和物种丰富度没有显著变化,而肺螺亚纲、前鳃亚纲和双壳纲的相对多度在蓝藻水华前后却又显著的不同。Lance[60]等对静水椎实螺(*Lymnaea stagnalis*)的研究发现,MC 使螺的生长变缓,这在幼年个体中更为显著,而成年个体的繁殖能力降低,没有发现存活率和迁移的变化,同时螺体内消化腺发生了一些可逆的变化,在未进食有毒藻类 3 周后变化消失。Gérard[61]等发现有毒蓝藻的循环性增殖与腹足类群落生物的减少相吻合。Oberholster[62]等发现水体中微囊藻毒性的增加伴随着大型无脊椎动物中蛭纲、摇蚊科和颤蚓科丰度的增加,在远离蓝藻浮渣的地方大型无脊椎动物丰度较低但多样性却较高,这可能与较细无机颗粒对生境多样性的改变、腐殖质分解使可利用溶氧降低、大量悬浮颗粒物长时间存在使透光性降低、藻类浮渣释放毒素对大型无脊椎动物的毒性作用和浮渣对 pH 与营养盐浓度等指标的影响有关。

3.3　底栖动物对蓝藻毒素在食物网中的传播作用

相关研究得出,MC 能够在食物链中迁移,但没有生物放大现象[63]。Papadimitriou[64]等对食物网中不同组成部分中 MC 的分布和累积进行了研究,虽然没发现生物放大的证据,但是 MC 对动物和人类健康的威胁仍然存在。Kozlowsky-Suzuki[65]等研究了食物网中 MC 消费者浮游动物、十足目、软体动物、鱼类、乌龟和水鸟体内 MC 的浓度,结果表明大部分的初级消费者表现为生物稀释,研究中仅有浮游动物和以浮游动物为食的鱼类出现生物放大现象,这与 Ibelings[66]等的研究一致。基于对简单食物链模型(*Microcystis aeruginosa*→*Daphnia pulex*→*Chaoborus*)的研究,Laurén[67]等发现捕食含有毒微囊藻饲养水蚤的幽蚊死亡率更高。虽然生物链几乎不能累积 MC,但是 MC 却能够以底栖动物假粪的形式被鱼类摄取而进入食物链[68]。Poste 和 Ozersky[69]也发现贻贝可以通过两种方式将 MC 传递到更高的营养级,一是被底栖鱼类(如虾虎鱼)所捕食,再就是可以通过它们的生物沉积物间接被其它底栖无脊椎动物取食。同时,Lance[70]等通过喂食鱼类静水椎实螺消化腺发现,鱼类的各个器官都会检测到 MC,且含量按肝脏、肌肉、肾脏和鳃的顺序降低。

4　讨论

由于底栖动物为水体中有毒物质的最直接接触者,目前关于底栖动物毒理学的研究已成为水环境毒理学研究的一个热点,经过多年的发展,已经获得了很多重要成果,但关于水华蓝藻毒素对底栖动物的毒理学研究仍然存在许多的问题需要进一步的研究,而今后最值得关注的问题主要有以下几个方面:

(1)毒素分析方法等的标准化　在对毒素近几十年的研究中,发展了许多检测分析毒素的方法,但由于毒素种类和异构体繁多、水体其它有毒物质干扰和检测仪器设备等问题,使得各种方法在实际的应用中存在一定的局限性,从而导致目前国际上还没有检测毒素的标准方法。同时,由于人类接触的毒素为各种毒素的混合,而目前对人体每天摄入量的规定只限于单一的毒素种类,对水产品的中含量的限定亦没有标准,所以对毒素监测分析方法和摄入量标准的研究仍会是今后研究的重要方向。

(2)加强蓝藻毒素对底栖动物致毒的分子机理和急性与慢性中毒反应,以及不同毒素之间的协同关系的研究　在重点研究微囊藻毒素的同时,还应加大对其他种类毒素的研究。同时,还应对蓝藻毒素进行长期的观测,进一步研究蓝藻毒素在底栖动物体内富集、转化、代谢以及沿食物链的传递机制,并筛选藻毒素污染指示生物,从而为进一步监测和评价其对人类健康的威胁提供证据。

(3)底栖动物对蓝藻毒素清除机制的研究　目前,相关研究已经证明底栖动物中的一些贝类对蓝藻毒素有很高的富集与清除能力,而贝类具有生物量大、滤食能力强、易于存活等特点,重要的是其中一些贝类具有很高的抗毒能力,所以对底栖动物清除蓝藻毒素机制的研究,对有毒蓝藻水华的防范与控制具有重要的意义。

(4)进一步加强对水体富营养化的研究　蓝藻毒素都是由藻类所产生,所以控制蓝藻毒素的关键最后还要依靠对水体富营养化的治理,既淡水水体水华各方面的研究仍是今后的热点。

(5)加强对一些最新研究方向的研究　主要有两个方面,一方面是关于一些药物对蓝藻毒素毒性作用的缓解作用的研究,如已有研究表明抗生素利福平、免疫抑制剂环孢霉素 A[71]和抗氧化剂维生素 E[72]对 MC 的

生物毒性都有一定的缓解作用;二是对蓝藻毒素的利用,有研究发现微囊藻毒素能够促使肝癌细胞凋亡[73],这表明一些藻毒素有可能成为重要的抗癌药物,所以关于这方面的研究必将成为一个新的热点。

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