◆ 综述与进展 ◆

农药环境污染对两栖动物蛙类毒性效应研究进展

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摘要：从农药对两栖动物的急性毒性、生长发育、行为活动、氧化应激、代谢器官及免疫系统等方面总结了近年来两栖动物毒性的研究情况，探讨了环境中农药对两栖动物的伤害，为评估农药对两栖动物带来的风险、制定科学有效的农药监管政策及良好GAP下农药高效合理使用方法提供了科学依据。

关键词：农药；两栖动物；蛙类；毒性效应

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Research Progress on the Toxic Effects of Pesticide Environment Pollution on Amphibian Frogs

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Abstract: This paper describes the research on amphibians under pesticide stress in recent years，and elaborates on the acute toxicity，growth and development，behavioral activities，biochemical and physicochemical effects，metabolic organs，and immune systems of pesticides on amphibians，the damage caused by pesticides to amphibians in the environment has been identified，which provides a scientific basis for assessing the risks posed by pesticides to amphibians，formulating scientific and effective pesticide regulatory policies，and establishing efficient and reasonable methods for pesticide use under the GAP.

Key words: pesticides; amphibians; frogs; toxic effects

农药是农、林、牧业中控制有害生物和调节植物生长的化学药品[1]。研究报道，若不施用农药，水果、蔬菜和谷物产量将分别减少78%、54%和32%[2]。因此，农药在提高全球农作物产量、提供充足的优质食品和缓解贫困等方面做出了重大贡献[3]。据统计，全球每年使用农药约30亿kg，但能有效控制害虫的总量只有1%[4]。大量的农药通过喷洒[5]、径流或渗流[6]等方式广泛分布于环境中，污染了水生和陆地环境，对非靶标生物构成一定的威胁。

两栖动物是维持水生、陆地和农田生态系统的非靶标生物，对平衡生态系统和保障粮食安全具有重要的意义[7]。然而两栖动物皮肤具有渗透性[8]，对环境化学物质较敏感，在水生和陆地栖息地接触农药的风险较高[9]。研究发现环境中的农药会显著影响两栖动物的发育[10]，导致平衡生态系统中两栖动物减少[11]，威胁了两栖动物的种群，削弱了两栖动物在生态系统中的功能。蛙类是常见的两栖动物，它们在食物链中发挥着重要的作用，每年捕食数以亿计的昆虫，是环境健康的重要指标。当污染物影响栖息地时，它们往往是第一批受害者，为生态系统中的敏感生物提供了预警。因此，研究农药对两栖动物的风险具有重要意义。

为了更好地保护两栖动物，实现人类活动和自然的和谐统一，本文根据近年来农药对两栖动物影响研究的文献，将农药对两栖动物的毒性效应进行了总结和分析，为评估农药对两栖动物的风险及农

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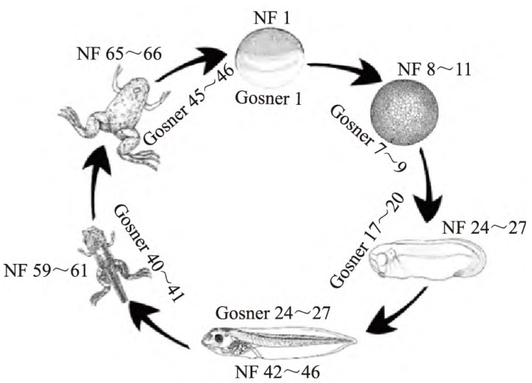
药的合理使用提供科学依据。

1　农药环境污染物对蛙类急性毒性研究

蛙类是农业害虫的主要天敌之一[12]，其典型的发育阶段如图1所示[13-14]。急性毒性试验是评估农药对非靶标生物造成影响的重要手段，通过LC_{50}（半致死浓度）可以快速有效地评价毒性，为长期慢性毒理试验、生殖毒性试验等提供基础数据[15]。当前，国内外学者就农药对蛙类急性毒性试验的数据见表1。



NF：模式生物非洲爪蟾的发育阶段
Gosner：无尾目两栖动物的发育阶段

图 1　蛙类典型发育周期

不同类别的农药对两栖动物产生的毒性不同。根据GB/T 31270.18—2014《化学农药环境安全评价试验准则》第18部分“天敌两栖类急性毒性试验”中农药对两栖动物的急性毒性划分，96 h的LC_{50}≤0.1 mg/L为剧毒，0.1＜LC_{50}≤1.0 mg/L为高毒，1.0＜LC_{50}≤10 mg/L为中毒，LC_{50}＞10 mg/L为低毒。

拟除虫菊酯、有机氯、有机磷类杀虫剂对蛙类的毒性大多表现为高毒，与其他发育阶段相比，对蝌蚪阶段的毒性更大；氨基甲酸酯杀虫剂对蛙类毒性研究较少，从文献上看，不同的氨基甲酸酯杀虫剂对蛙类毒性表现不一，灭多威对蝌蚪表现为低毒，甲萘威对成蛙毒性较高；新烟碱杀虫剂对蛙类毒性的研究大多集中在蝌蚪发育阶段，该阶段毒性为低毒，对胚胎和蛙阶段的研究较少；多数除草剂类农药对蛙的胚胎、蝌蚪、蛙发育阶段表现为中毒。杀菌剂品种繁多，结构不一，对非靶标生物有着不同的选择性，对蛙类的毒性研究集中在蝌蚪发育阶段，不同的杀菌剂对蝌蚪表现出显著差异的急性毒性，如肟菌酯对非洲爪蟾蝌蚪表现为低毒，而吡唑醚菌酯对美国牛蛙蝌蚪毒性达到了剧毒。

从毒性数据上发现，①对于同一种两栖动物，同一类型的不同种农药表现的毒性差异很大，如久效磷对Boana xerophylla蝌蚪的毒性为低毒，二嗪磷为中毒，而毒死蜱为高毒。同一农药对不同发育阶段两栖动物体现的毒性也存在着差异，如Roundup-草甘膦（有效成分为异丙胺盐）对非洲爪蟾蝌蚪表现为高毒，对胚胎和成蛙为中毒；硫丹对非洲爪蟾蝌蚪也表现为高毒性，而胚胎为中毒。②手性农药对两栖动物的毒性存在着显著差异，S-联苯菊酯对非洲爪蟾蝌蚪为高毒，而R-联苯菊酯为中毒，但手性农药对两栖动物毒性研究报道较少，应加强对该类农药的关注。多种毒性数据显示，两栖动物幼体阶段比胚胎对环境中的农药更为敏感，这可能是胚胎外层胶膜的存在使其免受化学品的污染[16]。

表 1　农药对两栖动物蛙类急性毒性试验数据

农药类别	农药	两栖动物类别	发育阶段	LC_{50}/(mg/L)	毒性等级
拟除虫菊酯杀虫剂	氯氰菊酯[17]	Physalaemus Gracilis	Gosner 17～18	117.41	低毒
		Physalaemus Gracilis	Gosner 24～25	5.01	中毒
	溴氰菊酯[17]	Physalaemus Gracilis	Gosner 17～18	3.04	中毒
		Physalaemus Gracilis	Gosner 24～25	0.5	高毒
	α- 氯氰菊酯[18]	黑斑蛙	Gosner 25	1.86	中毒
	Rac-联苯菊酯[19]	非洲爪蟾	NF 42～44	0.156	高毒
	S-联苯菊酯[19]	非洲爪蟾	NF 42～44	0.219	高毒
	R-联苯菊酯[19]	非洲爪蟾	NF 42～44	0.041	剧毒
有机氯杀虫剂	三唑酮[20]	黑斑蛙	Gosner 25	25.97	低毒
	硫丹[21]	非洲爪蟾	NF 8～11	1.266	中毒
		非洲爪蟾	NF 46	0.121	高毒
有机磷杀虫剂	乐果[22]	砂质犀角蟾	Gosner 25	38.86	低毒
	久效磷[23]	Boana xerophylla	Gosner 25	124.21～554.01	低毒
	二嗪磷[23]	Boana xerophylla	Gosner 25	2.12～7.92	中毒
	毒死蜱[23]	Boana xerophylla	Gosner 25	0.41～1.85	中毒

（续表 1）

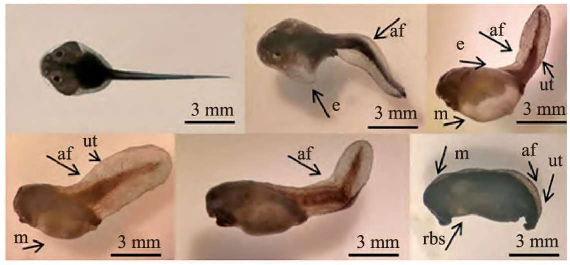
农药类别	农药	两栖动物类别	发育阶段	LC_{50}/(mg/L)	毒性等级
有机磷杀虫剂	毒死蜱[24]	蓝点蛙	Gosner 45～46	4.993	中毒
	马拉硫磷[20]	非洲爪蟾	NF 8～11	5.396	中毒
		非洲爪蟾	NF 46	6.756	中毒
	谷硫磷[25]	Hyalella curvispina	Gosner 45～46	0.166	高毒
氨基甲酸酯杀虫剂	克百威[26]	美国牛蛙	Gosner 31	29.9	低毒
	灭多威	亚洲蟾蜍[27]	Gosner 25	940.7	低毒
		棕色树蛙[27]	Gosner 25	380	低毒
		大理石侏儒蛙[27]	Gosner 25	84.57	低毒
		虎纹蛙[28]	Gosner 25	6.856	中毒
	甲萘威[29]	Hyalella curvispina	Gosner 45～46	0.213	高毒
新烟碱杀虫剂	噻虫嗪	中华蟾蜍[30]	Gosner 27～28	374.16	低毒
		Rhinella fernandezae[31]	Gosner 25～27	71.2	低毒
	吡虫啉	砂质犀角蟾[30]	Gosner 25～27	25.98	低毒
		Scinax granulatus[31]	Gosner 25～27	11.28	低毒
		非洲爪蟾[32]	NF 65～66	74.18	低毒
		黑斑蛙[33]	Gosner 25～26	173.55	低毒
	氟啶虫胺腈[33]	黑斑蛙	Gosner 25～27	427.37	低毒
	啶虫脒	黑斑蛙[34]	Gosner 25～28	18.49	低毒
		非洲爪蟾[35]	NF 65～66	64.48	低毒
		热带西爪蛙[36]	NF 49～50	>100	低毒
杀菌剂	肟菌酯[37]	非洲爪蟾	NF 46	13.41	低毒
	戊唑醇[16]	Physalaemus cuvieri	Gosner 25	0.98	高毒
	吡唑醚菌酯	美国牛蛙[38]	Gosner 26～28	0.010 6	剧毒
	百菌清	美国牛蛙[38]	Gosner 26～28	0.017 8	剧毒
		丽红眼蛙[39]	Gosner 26～27	0.026 6	剧毒
		日本树蟾[39]	Gosner 25～27	0.025 5	剧毒
		Smilisca baudinii[39]	Gosner 28～34	0.032 3	剧毒
除草剂	西玛津[40]	热带西爪蛙	NF 49～50	7.55	中毒
	莠去津[40]	热带西爪蛙	NF 49～50	1.54	中毒
	丁草胺[41]	泽蛙	Gosner 26	0.87	高毒
	Roundup- 草甘膦（有效成份异丙胺盐）[42]	非洲爪蟾	NF 8～11	1.05	中毒
			NF 48	0.89	高毒
			NF 60	2.75	中毒
	Kilo Max- 草甘膦（有效成分钠盐）[42]	非洲爪蟾	NF 8～11	207	低毒
			NF 48	58.1	低毒
			NF 60	455	低毒
	Enviro- 草甘膦（有效成分异丙胺盐）[42]	非洲爪蟾	NF 8～11	466	低毒
			NF 48	134.6	低毒
			NF 60	525.7	低毒
	嗪草酮[43]	Physalaemus cuvieri	Gosner 25	85	低毒
		Hypsiboas pardlis	Gosner 25	68	低毒
	敌草隆[44]	牛蛙	Gosner 25	31 ± 3.7	低毒
	西草净[45]	Silurana tropicalis	NF 49～50	16.9～3.7	低毒
	苯噻草胺[45]	Silurana tropicalis	NF 49～51	3.06～2.7	中毒
	禾草丹[45]	Silurana tropicalis	NF 49～52	1.77～0.725	中毒
	百草枯[46]	非洲蟾蜍	Gosner 25	6.49	中毒
	乙草胺	Physalaemus cuvieri[43]	Gosner 25	4.4	中毒
		Hypsiboas pardlis[44]	Gosner 25	7.8	中毒

2　农药环境污染物对蛙类发育的影响

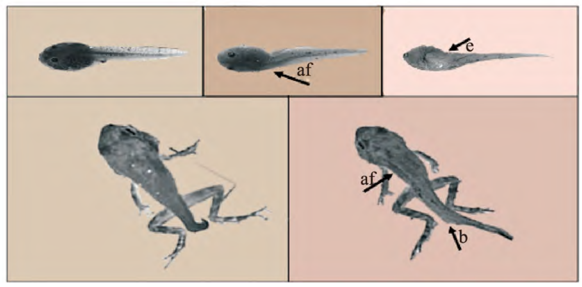
农药在减少害虫造成的作物损失方面发挥着关键作用，然而，残留在环境中的农药对两栖动物的生存造成了一定的危害，对两栖动物各个发育阶段表现出不同程度的损伤。

在胚胎阶段，西维因、硫丹和辛基苯酚降低了河边蝾螈的存活率[47]；百菌清的持续暴露抑制了阿根廷蟾蜍的孵化率，并造成其腹部和尾畸形[48]；百草枯导致蟾蜍发育停滞，头和背部畸形明显[49]。在幼体阶段，噻虫嗪和氯噻嗪抑制了非洲爪蟾蝌蚪体重和体长的发育[50]；暴露于氯氰菊酯仅168 h对蟾蜍产生的畸形指数就达到了5[51]；毒死蜱严重损害了黑眼睑小树蛙口腔及肠的结构[52]，导致捷蛙的骨骼和肌肉缺失，改变了鳃的形态和超微结构，蝌蚪依靠鳃呼吸，而影响鳃的发育会导致其呼吸困难，对蝌蚪健康和体能造成一定的影响[53]；西草净不仅延迟了Silurana tropicalis后肢的发育，还造成尾扭曲严重[54]；阿特拉津的胁迫降低了南方豹蛙发育阶段的生长率，造成按时变态的蝌蚪较少[55]；硫丹的暴露导致了变态后Fejervarya sp.1 和F.teraiensisd前后肢的畸形[56]；西维因使南方豹蛙在变态发育过程中有较高的死亡率，且近18%的豹蛙出现了畸形，包括内脏和四肢等[57]，同时农场中发现成年阶段草蛙和湍雨滨蛙的前肢和后肢不完整[58]；毒死蜱、乐果和敌稗的暴露导致沙漏树蛙的脊柱侧弯、后凸，以及水肿和皮肤溃疡等损伤[59]。研究还发现农药对两栖动物妊娠母体有一定的毒性。农药污染池中暴露程度更高的蟾蜍种群长期存在生殖障碍——受精、存活率低等问题[60]。农药对蛙类常见的形态损伤见图2，图中af表示轴弯曲，e为水肿，b为尾畸形，m为头畸形，rbs为体型缩小，ut为尾发育不全[52,54]。

生物生长过程受基因在时间、空间上高度有序表达的调控。农药散播在环境中，可能会干扰两栖动物发育相关基因的表达，影响基因的功能，造成包括畸形在内的各种发育异常。如草甘膦暴露于非洲爪蟾胚胎后，心脏中isl1（胰岛素增强子结合蛋白1）、nkx2.5（心脏特异性同源盒转录因子）、mhca（α-肌球蛋白重链）、actc1（心肌α-肌动蛋白）和tnni3（肌钙蛋白I）表达降低，心脏结构异常，导致心率降低[61]。在有机锡的暴露下，非洲爪蟾甲状腺应答基因trβ（甲状腺激素受体β）、bteb（基本转录元件结合蛋白）、dio2（碘甲腺原氨酸脱碘酶-2）、tshβ（促甲状腺激素β亚基）和slc5a5（溶质载体家族成员5）的表达受到影响，扰乱了甲状腺的信号通路，抑制了甲状腺的发育[62]；在甲萘威的作用下，绿蛙蝌蚪甲状腺的应答基因表达受到抑制，影响了其在mRNA中的丰度分布[63]。



(a) 蟾蜍



(b) 捷蛙

图 2　农药胁迫下对蛙类形态常见的损伤

3　农药环境污染物对蛙类行为活动的影响

动物的行为（觅食、社交、交配、捕食、迁徙和躲避）是评价动物及其种群状态的标志[64]。两栖动物具备独特的生理特性，在食物链中有着重要的地位，而农药的广泛使用对其生存、捕食和繁殖造成了一定的影响，进而危害了其种群和生态系统的平衡。

异常旋转和不正确姿势是神经毒性应激的标志之一[65]。在硫丹的暴露下，斑点蛙蝌蚪表现出尾旋转快速、侧卧及背部向下等异常行为[6]；灭多威的暴露使得阿拉伯蟾蜍蝌蚪也出现类似的情况[66]。

食物是动物生长及生理功能的必需品[67]。西维因导致南方蟾蜍蝌蚪进食量减少了40%[68]；噁唑酰草胺对非洲爪蟾蝌蚪摄食有显著的抑制作用[69]。觅食的减少会导致用于分配储存、繁殖和生长的能量受到限制[70]，对健康造成影响。

游泳模式是评估蝌蚪生态毒理学行为活动的一种典型方式[71]。南方豹蛙蝌蚪游泳的总位移和平均速度随着噻虫胺暴露浓度的增加而显著下降[72]；敌草隆的暴露显著降低了牛蛙蝌蚪的最大速度[44]。在视觉测定和视频跟踪模式下，发现硫丹对非洲爪蟾蝌蚪游泳行为造成了影响，且导致其取食次数降低[73]。草甘膦的暴露降低了捷蛙蝌蚪躲避蜻蜓幼虫的能力[74]；模拟苍鹭攻击的环境，发现暴露于吡虫啉

的林蛙难以逃离捕食者的追捕，而没有接触吡虫啉的林蛙会通过移动和跳跃等方式来躲避[75]。

交配行为也会因农药污染物受到影响。接触莠去津的雄性非洲爪蟾睾丸酮降低、繁殖腺变小、喉部发育雌性化，导致交配行为受到影响，从而降低了它们的生育能力[76]。

除此以外，研究表明农药产生的毒性效应可能会干扰两栖动物的自主神经调控，从而影响其行为。2，4-二氯苯氧乙酸能够降低牛蛙蝌蚪的呼吸速率[77]，硫丹的暴露降低了青蛙蝌蚪在水面呼吸的频次[78]，而充足的水面呼吸对于调节两栖动物的血氧有着重要的意义[6]。

4　农药环境污染物对蛙类氧化应激的影响

氧化应激是指体内氧化与抗氧化作用失衡的状态，一般主要是指自由基在体内产生的一种负面作用，是导致衰老和疾病的一个重要因素[79]。自由基会产生氧化应激现象，该现象对脂质、蛋白质、DNA及外源抗氧系统的酶系统和非酶系统都会产生负面影响[80]，如图3所示。

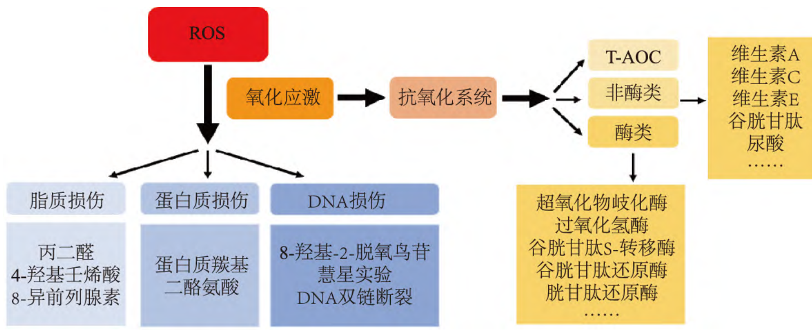


图 3　产生氧化应激的自由基途径

丙二醛（MDA）是脂质过氧化反应产生的代谢产物，其含量可反映脂质过氧化水平，即机体细胞受自由基攻击的程度。在噻虫嗪的影响下，中华蟾蜍蝌蚪体内丙二醛含量显著升高，造成了脂质过氧化[33]；随着暴露时间的持续，戊唑醇使黑斑蛙体内MDA含量持续升高[81]。蛋白质羰基是多种氨基酸在蛋白质氧化修饰过程中的早期标志，其含量高低表明蛋白质氧化损伤程度的大小，是衡量蛋白质氧化损伤的主要指标[82]。敌百虫的暴露不仅使Boana curupi蝌蚪体内MDA升高，而且增加了蛋白质羰基的含量，诱导了脂质、蛋白质的氧化损伤[83]。在彗星实验中，根据Endo III sites位点计算分析草甘膦和草膦酸铵对砂质犀角蟾蝌蚪是否造成DNA损伤，结果表明两种农药均造成蝌蚪的DNA损伤，其中草甘膦引起的氧化损伤更为严重[84]。

抗氧化系统主要分为酶类抗氧化系统和非酶类抗氧化系统，其使自由基的产生与消除处于动态平衡状态，是生物体的一种适应性机制。抗氧化酶从不同角度协助清除体内的活性氧（ROS），在抗氧化过程中起着重要的作用[85]。超氧化物歧化酶（SOD）和过氧化氢酶（CAT）是抗氧化系统的核心组成部分，在防御氧自由基方面起着不可或缺的作用[86]；谷胱甘肽S-转移酶(GST)是一种已知的II相代谢解毒酶，可催化谷胱甘肽（GSH）与外源物质及其代谢产物相结合[87]。热带爪蟾胚胎暴露于低浓度高效氯氟氰菊酯后，随着浓度的增加，SOD和GST活性显著升高，诱导氧化应激[88]；黑斑蛙蝌蚪在高剂量吡虫啉暴露下，体内SOD、CAT、GST活性降低[32]。分析其原因，可能是ROS过度积累，导致这些酶无法抵御高水平的氧化应激，从而失去活性[89]。在阿特拉津和毒死蜱的胁迫下，东北林蛙变态时期肝脏组织中的SOD和CAT活性随着农药剂量的上升而显著下降[90]；非洲爪蟾幼蛙暴露于啶虫脒导致SOD、CAT、GST活性增加[35]；农药诱导的GST和CAT活性存在性别差异，成年雌雄非洲爪蟾暴露于三唑酮及其代谢物三唑醇，发现对雌性血液中SOD的影响大于雄性，与GST和CAT的结果相反[91]。农药的暴露也会改变其他抗氧化酶的活性。GR（谷胱甘肽还原酶）是生物体中去除过量ROS的抗氧化酶，可以促进生物体细胞的健康发育[92]。黑斑蛙蝌蚪暴露于吡虫啉后，GR活性显著升高[93]。T-AOC（总抗氧化能力）是机体抗氧化系统功能状态的综合能力，其大小直接反映机体清除自由基的总体能力[87]，对机体T-AOC的检测可以直观地反映环境化学物质对生物体生理毒性的影响程度。随着啶虫脒和噻虫嗪浓度的升高和持续暴露，镇海林蛙蝌蚪体内的T-AOC受到抑制并逐渐下

降，对蝌蚪的抗氧化系统造成了毒害作用[94]。

非酶类抗氧化剂GSH（谷胱甘肽）是多种酶的辅酶，涉及多种生物学过程，参与清除ROS，防护氧化应激对机体产生的损伤[95]。研究发现，蟾蜍的GSH不受甲萘威的胁迫，这可能是由于CAT被抑制，从而维持了GSH水平的结果[96]。NO是一种高活性、膜可渗透的自由基，也是一种重要的信号分子和非酶抗氧化剂[97]。戊唑醇暴露于变态期非洲爪蟾，导致其NO水平下降[98]，ROS会氧化NO合成酶的辅因子，减少其活性，使NO含量降低[100]。

5　农药环境污染物对蛙类代谢器官的影响

代谢是生物体从环境中摄取营养物质转化为自身物质，同时将自身原有组成物转变为废物排出到环境的不断更新的过程。肝脏和肾脏是维持两栖动物正常功能的重要代谢器官。

肝脏有着强大的解毒、代谢、免疫的生理功能，肝脏通过肝药酶清除血液中的废物和外来异物，防止肝损伤以维持生命的正常活动[100]，因此，肝脏是某些农药对非靶标动物毒性的主要靶器官[101]。据报道，检测农田中的两栖动物，仅在其肝脏内就检测出9种农药[102]。农药造成的肝脏毒性主要决定于暴露强度、影响的细胞类型以及化合物的暴露时间。常见的肝损伤类型主要有肝细胞死亡、胆汁淤积、胆管损伤、肝血窦异常、脂肪肝、肝纤维化、肝硬化和肝肿瘤等。戊唑醇和乙胺嘧啶对意大利树蛙蝌蚪肝脏表现出不同的损伤，戊唑醇对肝脏表现出肝变质和肝细胞的间隙扩张[103]；乙胺嘧啶暴露导致意大利树蛙血管扩张及窦充血明显[104]；西玛津可导致非洲爪蟾蝌蚪肝细胞坏死及萎缩[105]；在吡虫啉的作用下，发现炎症细胞聚集在非洲爪蟾幼蛙的肝组织中[35]。三唑酮及其代谢物三唑醇对非洲爪蟾成蛙的肝脏造成肝质膜溶解、肝窦轻度扩张及细胞索结构疏松等损伤[91]；接触敌百虫后的树蛙，发现其肝细胞空泡化、坏死和肿胀[106]；溴氰菊酯增加了沼泽蛙肝脏黑素吞噬聚集物，肝窦扩张、浸润、血管上皮、中央静脉变性等病变[107]；在施用农药的稻田中发现*Lysapsus limellum*和*Rhinella bergi*肝窦增大、血运过度、肝细胞空泡化和血管扩张等现象[108]；林蛙接触毒死蜱后，肝纤维化突出[109]，而肝纤维化是慢性肝损伤的病理特征[110]。肝细胞毒性生物标志物是评价肝损伤的重要手段，如丙氨酸转移酶、天冬氨酸转移酶、山梨醇脱氢酶、谷氨酸脱氢酶等。啶虫脒引起了埃及蟾蜍血清中肝功能酶活性异常[111]。

两栖动物在新陈代谢过程中会产生多种废物，大部分废物通过肾小球滤过、肾小管的重吸收及分泌功能排出，同时排出体内的多余水分，以此调节体内的酸碱平衡，并维持内环境的稳定[112]。而污染物在两栖动物体内的堆积会破坏以上平衡，对肾脏产生负面的影响[113]。常见的肾脏损伤有水肿、肾小管扩张、单核细胞浸润、肾小管上皮细胞变性、出血及纤维化等。在敌百虫的胁迫下林蛙蝌蚪外观浮肿严重，解剖后发现其鳃腔内充水，肾脏器官颜色异常呈灰白色[114]；戊唑醇的暴露造成意大利树蛙蝌蚪肾脏炎症，并导致肾小管扩张、出血及单核细胞浸润等损伤[104]；溴氰菊酯造成沼泽蛙肾脏肾小球收缩、肾小管上皮细胞变性、肾小囊细胞肥大等一系列问题[106]；在西维因的暴露下，在蟾蜍的肾脏中观察到肾小管上皮变形、空泡化、核溶解、坏死、出血及纤维化[115]。除此以外，研究还发现农药的存在会抑制肾脏的发育，敌敌畏的暴露，抑制了斑腿泛树蛙肾脏的发育，导致其肾脏萎缩[116]。

6　农药环境污染物对蛙类免疫系统的影响

免疫是阻止机体受到病原体攻击的一种防护措施[117]。两栖动物暴露于农药后，免疫系统是其抵抗外来物质的重要场所[118]。农药对两栖动物免疫系统的直接或者间接损害，将导致免疫细胞发生变化，进而影响机体的免疫反应。注射炎症介质巯基乙酸，白细胞数量显著减少，且其吞噬活性减弱与炎症介质巯基乙酸模型相比，低浓度的莠去津对北方豹蛙也产生了类似的作用，表现为白细胞数量减少，吞噬活性降低，降低了炎症反应的应答[119]；北方豹蛙和非洲爪蟾暴露于6种混合农药后，对寄生虫的抗性减弱，其中豹蛙蝌蚪中淋巴细胞数量显著减少[120]，爪蟾蝌蚪中脾细胞和吞噬细胞数量显著减少[121]。

农药的暴露，对免疫细胞相关酶也造成了一定的影响，它们是维持脊椎动物机体免疫系统功能重要的酶[122]。在倍硫磷和氧乐果的暴露下，青蛙组织中MPO（髓过氧化物酶）活性增加[123]。MPO是中性粒细胞释放的防止病原体侵入机体的一种酶，在生理过程下，病原菌侵入机体MPO形成次氯酸，促进吞噬溶酶体内所含微生物的破坏[124]。随着MPO活性的增加，产生的次氯酸促进了宿主组织损伤。

农药还可改变免疫基因的表达，不仅抑制了免疫反应，还增加了两栖动物感染寄生虫的风险。莠去津抑制了非洲爪蟾蝌蚪中与免疫功能相关的7个基因的表达[125]；氯氰菊酯和噻苯达唑长期暴露引起

非洲爪蟾蝌蚪线粒体热激蛋白hsp 70和IL-1b（白细胞介素1b）显著上升[126]。莠去津[127]和西维因[128]导致幼体和变态期的非洲爪蟾抗病毒能力减弱，蝌蚪在感染FV3（蛙病毒3型）病毒后死亡率增加，炎性因子TNF-α和抗病毒基因IFN-I（I型干扰素）发生显著改变。

7 结论和展望

环境中的农药污染了两栖动物的栖息地，损伤了两栖动物的黏膜、皮肤、组织和器官，影响了两栖动物的变态发育和生长发育过程，降低了两栖动物的免疫能力，使两栖动物的行为活动受限，躲避天敌、捕食、繁殖的能力下降。高效、低毒、低残留的化学农药一直是开发绿色农药和环境友好农药的准则，技术、防控手段和方式的不断改进可以减少化学农药使用的途径，制定科学、合理有效的农药使用准则和规范，评估农药对两栖动物的风险，防止农药在环境中的污染及对非靶标生物造成的影响，对在全球两栖动物数量锐减的背景下更好地保护两栖动物具有重要意义。

参考文献

[1] World Health Organization . International code of conduct on pesticide management: guidelines on highly hazardous pesticides [R].Geneva: Food & Agriculture Organization, 2018.

[2] LAMICHHANE J R. Pesticide use and risk reduction in European farming systems with IPM: an introduction to the special issue[J]. Crop Protection, 2017, 97: 1-6.

[3] STRASSEMEYER J, DAEHMLOW D, DOMINIC A R, et al. SYNOPS-WEB, an online tool for environmental risk assessment to evaluate pesticide strategies on field level[J]. Crop Protection, 2017, 97: 28-44.

[4] HAYES T B, HANSEN M. From silent spring to silent night: agrochemicals and the anthropocene[J]. Elementa: Science of the Anthropocene, 2017, 5: 57.

[5] BRÜHL C A, SCHMIDT T, PIEPER S, et al. Terrestrial pesticide exposure of amphibians: an underestimated cause of global decline? [J]. Scientific Reports, 2013, 3(1): 1135.

[6] LAVORATO M, BERNABO I, CRESCENTE A, et al. Endosulfan effects on Rana dalmatina tadpoles: quantitative developmental and behavioural analysis[J]. Archives of Environmental Contamination and Toxicology, 2013, 64: 253-262.

[7] 曹玲, 刘沁雨, 郑豪杰, 等. 农药对两栖动物的生态风险评估研究进展[J]. 农药学学报, 2021, 23(3): 456-468.

[8] LANCTÔT C M, CRESSWELL T, MELVIN S D. Uptake and tissue distributions of cadmium, selenium and zinc in striped marsh frog tadpoles exposed during early post-embryonic development [J]. Ecotoxicology and Environmental Safety, 2017, 144: 291-299.

[9] KHAN M Z, LAW F C P. Adverse effects of pesticides and related chemicals on enzyme and hormone systems of fish, amphibians and reptiles: a review[J]. Proceedings of the Pakistan Academy of Sciences, 2005, 42(4): 315-323.

[10] STUART S N, CHANSON J S, COX N A, et al. Status and trends of amphibian declines and extinctions worldwide[J]. Science, 2004, 306(5702): 1783-1786.

[11] FILLIOE S, BISHOP K K, JANNINI A V S, et al. In vivo, noncontact, real-time, PV [O] H imaging of the immediate local physiological response to spinal cord injury in a rat model [J]. Journal of Biomedical Optics, 2020, 25(3): 32007.

[12] 丁建发. 试论蛙类生活习性的多样性[J]. 宁德师专学报(自然科学版), 2004(4): 361-363.

[13] GOSNER K L. A simplified table for staging anuran embryos and larvae with notes on identification[J]. Herpetologica, 1960, 16(3): 183-190.

[14] XENBAS E. Xenopus laevis stage series: complete [EB/OL]. [2023-09-20]. http: //www.xenbase.org/anatomy/a-lldev.do

[15] BRADFORD D F, KNAPP R A, SPARLING D W, et al. Pesticide distributions and population declines of California, USA, alpine frogs, Rana muscosa and Rana sierrae[J]. Environmental Toxicology and Chemistry, 2011, 30(3): 682-691.

[16] WRUBLESWSKI J, REICHERT F W, GALON L, et al. Acute and chronic toxicity of pesticides on tadpoles of Physalaemus cuvieri (Anura, Leptodactylidae)[J]. Ecotoxicology, 2018, 27: 360-368.

[17] MACAGNAN N, RUTKOSKI C F, KOLCENTI C, et al. Toxicity of cypermethrin and deltamethrin insecticides on embryos and larvae of Physalaemus gracilis (Anura: Leptodactylidae)[J]. Environmenta l Science and Pollution Research, 2017, 24 (25): 20699-20704.

[18] XU P, HUANG L. Effects of α -cypermethrin enantiomers on the growth, biochemical parameters and bioaccumulation in Rana nigromaculata tadpoles of the anuran amphibians[J]. Ecotoxicology and Environmental Safety, 2017, 139: 431-438.

[19] ZHANG W, CHEN L, DIAO J, et al. Effects of cis-bifenthrin enantiomers on the growth, behavioral, biomarkers of oxidative damage and bioaccumulation in Xenopus laevis[J]. Aquatic Toxicology, 2019, 214: 105237.

[20] ZHANG W, LU Y, HUANG L, et al. Comparison of triadimefon and its metabolite on acute toxicity and chronic effects during the early development of Rana nigromaculata tadpoles[J]. Ecotoxicology and Environmental Safety, 2018, 156: 247-254.

[21] YU S, WAGES M R, CAI Q, et al. Lethal and sublethal effects of three insecticides on two developmental stages of Xenopus laevis and comparison with other amphibians[J]. Environmental Toxicology and Chemistry, 2013, 32(9): 2056-2064.

[22] ACQUARONI M, PELUSO J, SVARTZ G, et al. Characterization of acute toxicity, genotoxicity, and oxidative stress of dimethoate in Rhinella arenarum larvae[J]. Environmental Science and Pollution Research, 2021, 28: 41772-41779.

[23] HENAO L M, MENDEZ J J, BERNAL M H. UVB radiation enhances the toxic effects of three organophosphorus insecticides on tadpoles from tropical anurans[J]. Hydrobiologia, 2022, 849(1): 141-153.

[24] SRIVASTAV A K, SRIVASTAVA S, SRIVASTAV S K, et al. Acute toxicity of an organophosphate insecticide chlorpyrifos to an anuran, Rana cyanophlyctis[J]. Iranian Journal of Toxicology, 2017, 11(2): 45-49.

[25] ANGUIANO O L, CASTRO C, VENTURINO A, et al. Acute toxicity and biochemical effects of azinphos methyl in the amphipod Hyalella curvispina[J]. Environmental toxicology, 2014, 29(9): 1043-1053.

[26] FRANÇA F M, BRAZIL DE P T C, MARCANTÔNIO A S, et al. Acute toxicity and ecotoxicological risk assessment of rice pesticides to Lithobates catesbeianus tadpoles[J]. Journal of Environmental Science and Health: Part B, 2015, 50(6): 406-410.

[27] LAU E T C, KARRAKER N E, LEUNG K M Y. Temperature-dependent acute toxicity of methomyl pesticide on larvae of 3 Asian amphibian species[J]. Environmental Toxicology and Chemistry, 2015, 34(10): 2322-2327.

[28] TRACHANTONG W, SAENPHET S, SAENPHET K, et al. Lethal and sublethal effects of a methomyl-based insecticide in Hoplobatrachus rugulosus[J]. Journal of Toxicologic Pathology, 2017, 30(1): 15-24.

[29] ANGUIANO O L, VACCA M, ARAUJO M E R, et al. Acute toxicity and esterase response to carbaryl exposure in two different populations of amphipods Hyalella curvispina[J]. Aquatic Toxicology, 2017, 188: 72-79.

[30] 陈姣姣, 陈晓芳, 郑书梅, 等. 噻虫嗪对中华蟾蜍蝌蚪抗氧化系统及丙二醛含量的影响[J]. 福建师范大学学报(自然科学版), 2019, 35(5): 61-66.

[31] FONSECA P, SHIRLEY V D, GUILLERMO S N, et al. Toxicity of the neonicotinoid insecticides thiamethoxam and imidacloprid to tadpoles of three species of South American amphibians and effects of thiamethoxam on the metamorphosis of Rhinella arenarum[J]. Journal of Toxicology and Environmental Health: Part A, 2022, 85(24): 1019-1039.

[32] ZHOU X, MING R Y, GUO M T, et al. Characterization of imidacloprid-induced hepatotoxicity and its mechanisms based on a metabolomic approach in Xenopus laevis[J]. Science of the Total Environment, 2023, 869: 161794.

[33] ZHOU X, DENG Y, WANG R, et al. Toxic effects of imidacloprid and sulfoxaflor on Rana nigromaculata tadpoles: growth, antioxidant indices and thyroid hormone-related endocrine system [J]. Arabian Journal of Chemistry, 2023, 16(6): 104723.

[34] GUO W, YANG Y, ZHOU X, et al. Insight into the toxic effects, bioconcentration and oxidative stress of acetamiprid on Rana nigromaculata tadpoles[J]. Chemosphere, 2022, 305: 135380.

[35] JIAO H, YUAN T, WANG X, et al. Biochemical, histopathological and untargeted metabolomic analyses reveal hepatotoxic mechanism of acetamiprid to Xenopus laevis[J]. Environmental Pollution, 2023, 317: 120765.

[36] SAKA M, TADA N. Acute and chronic toxicity tests of systemic insecticides, four neonicotinoids and fipronil, using the tadpoles of the western clawed frog Silurana tropicalis[J]. Chemosphere, 2021, 270: 129418.

[37] UÇKUN M, ÖZMEN M. Evaluating multiple biochemical markers in Xenopus laevis tadpoles exposed to the pesticides thiacloprid and trifloxystrobin in single and mixed forms[J]. Environmental Toxicology and Chemistry, 2021, 40(10): 2846-2860.

[38] HOPKINS A P, HOVERMAN J T. Acute aquatic toxicity of two commonly used fungicides to midwestern amphibian larvae [J]. Ecotoxicology, 2023, 32(2): 188-195.

[39] MÉNDEZ M, OBANDO P, PINNOCK-BRANFORD M, et al. Acute, chronic and biochemical effects of chlorothalonil on Agalychnis callidryas, Isthmohyla pseudopuma and Smilisca baudinii tadpoles[J]. Environmental Science and Pollution Research, 2016, 23: 21238-21248.

[40] SAKA M, TADA N, KAMATA Y. Chronic toxicity of 1, 3, 5-triazine herbicides in the postembryonic development of the western clawed frog Silurana tropicalis[J]. Ecotoxicology and Environmental Safety, 2018, 147: 373-381.

[41] LIU W Y, WANG C Y, WANG T S, et al. Impacts of the herbicide butachlor on the larvae of a paddy field breeding frog (Fejervarya limnocharis) in subtropical Taiwan[J]. Ecotoxicology, 2011, 20: 377-384.

[42] BABALOLA O O, VAN WYK J H. Comparative early life stage toxicity of the African clawed frog, Xenopus laevis following exposure to selected herbicide formulations applied to eradicate alien plants in South Africa[J]. Archives of Environmental Contamination and Toxicology, 2018, 75: 8-16.

[43] DAAM M A, MOUTINHO M F, ESPí NDOLA E L G, et al. Lethal toxicity of the herbicides acetochlor，ametryn，glyphosate and metribuzin to tropical frog larvae[J]. Ecotoxicology, 2019, 28: 707-715.

[44] MOREIRA R A, FREITAS J S, DA SILVA P T J, et al. Mortality, spatial avoidance and swimming behavior of bullfrog tadpoles (Lithobates catesbeianus) exposed to the herbicide diuron [J]. Water, Air & Soil Pollution, 2019, 230: 1-12.

[45] SAKA M. Acute toxicity of rice paddy herbicides simetryn, mefenacet, and thiobencarb to Silurana tropicalis tadpoles [J]. Ecotoxicology and Environmental Safety, 2010, 73(6): 1165-1169.

[46] UMEOKEKE H C, AMAEZE H N, EHIGUESE F O, et al. Dichlorvos and Paraquat induced avoidance responses in tadpoles (Amietophrynus regularis reuss, 1833) and their contribution to population decline[J]. Environmental Analysis, Health and Toxicology, 2022, 37(2): DOI: 10.562 o/eaht. 2022017.

[47] ROHR J R, ELSKUS A A, SHEPHERD B S, et al. Lethal and sublethal effects of atrazine, carbaryl, endosulfan, and octylphenol on the streamside salamander (Ambystoma barbouri)[J]. Environ-

mental Toxicology and Chemistry: An International Journal, 2003, 22(10): 2385-2392.

[48] ACQUARONI M, SVARTZ G, PÉREZ COLL C. Developmental toxicity assessment of a chlorothalonil-based fungicide in a native amphibian species[J]. Archives of Environmental Contamination and Toxicology, 2021, 80: 680-690.

[49] MUSSI M A, CALCATERRA N B. Paraquat-induced oxidative stress response during amphibian early embryonic development[J]. Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology, 2010, 151(2): 240-247.

[50] JENKINS J A, HARTOP K R, BUKHARI G, et al. Juvenile African clawed frogs (Xenopus laevis) express growth, metamorphosis, mortality, gene expression, and metabolic changes when exposed to Thiamethoxam and Clothianidin[J]. International Journal of Molecular Sciences, 2021, 22(24): 13291.

[51] SVARTZ G, ARONZON C, PÉREZ C C. Comparative sensitivity among early life stages of the South American toad to cypermethrin-based pesticide[J]. Environmental Science and Pollution Research, 2016, 23: 2906-2913.

[52] RUTKOSKI C F, MACAGNAN N, FOLADOR A, et al. Morphological and biochemical traits and mortality in Physalaemus gracilis (Anura: Leptodactylidae) tadpoles exposed to the insecticide chlorpyrifos[J]. Chemosphere, 2020, 250: 126162.

[53] BERNABÒ I, SPERONE E, TRIPEPI S, et al. Toxicity of chlorpyrifos to larval Rana dalmatina: acute and chronic effects on survival, development, growth and gill apparatus[J]. Archives of Environmental Contamination and Toxicology, 2011, 61: 704-718.

[54] SAKA M, TADA N, KAMATA Y. Application of an amphibian (Silurana tropicalis) metamorphosis assay to the testing of the chronic toxicity of three rice paddy herbicides: simetryn, mefenacet, and thiobencarb[J]. Ecotoxicology and Environmental Safety, 2013, 92: 135-143.

[55] ADELIZZI R, PORTMANN J, VAN METER R. Effect of individual and combined treatments of pesticide, fertilizer, and salt on growth and corticosterone levels of larval southern leopard frogs (Lithobates sphenocephala)[J]. Archives of Environmental Contamination and Toxicology, 2019, 77: 29-39.

[56] DEVI N N, GUPTA A. Toxicity of endosulfan to tadpoles of Fejervarya spp. (Anura: Dicroglossidae): mortality and morphological deformities[J]. Ecotoxicology, 2013, 22: 1395-1402.

[57] BRIDGES C M. Long-term effects of pesticide exposure at various life stages of the southern leopard frog (Rana sphenocephala)[J]. Archives of Environmental Contamination and Toxicology, 2000, 39: 91-96.

[58] SPOLYARICH N, HYNE R V, WILSON S P, et al. Morphological abnormalities in frogs from a rice-growing region in NSW, Australia, with investigations into pesticide exposure[J]. Environmental Monitoring and Assessment, 2011, 173: 397-407.

[59] JAYAWARDENA U A, ROHR J R, NAVARATNE A N, et al. Combined effects of pesticides and trematode infections on hourglass tree frog Polypedates cruciger[J]. EcoHealth, 2016, 13: 111-122.

[60] ADAMS E, LEEB C, BRÜHL C A. Pesticide exposure affects reproductive capacity of common toads (Bufo bufo) in a viticultural landscape[J]. Ecotoxicology, 2021, 30(2): 213-223.

[61] FLACH H, LENZ A, PFEFFER S, et al. Impact of glyphosate-based herbicide on early embryonic development of the amphibian Xenopus laevis[J]. Aquatic Toxicology, 2022, 244: 106081.

[62] LI S, QIAO K, JIANG Y, et al. Disruptive effects of two organotin pesticides on the thyroid signaling pathway in Xenopus laevis during metamorphosis[J]. Science of the Total Environment, 2019, 697: 134140.

[63] BOONE M D, HAMMOND S A, VELDHOEN N, et al. Specific time of exposure during tadpole development influences biological effects of the insecticide carbaryl in green frogs (Lithobates clamitans)[J]. Aquatic Toxicology, 2013, 130: 139-148.

[64] BROOMHALL S. Measuring chemical impacts on amphibians: ecotoxicity and behavioral data in governmental regulation [J]. Applied Herpetology, 2005, 2(3): 259-285.

[65] BRUNELLI E, BERNABÒ I, BERG C, et al. Environmentally relevant concentrations of endosulfan impair development, metamorphosis and behavior in Bufo bufo tadpoles[J]. Aquatic Toxicology, 2009, 91(2): 135-142.

[66] SELEEM A A. Teratogenicity and neurotoxicity effects induced by methomyl insecticide on the developmental stages of Bufo arabicus [J]. Neurotoxicology and Teratology, 2019, 72: 1-9.

[67] EGEA-SERRANO A, TEJEDO M, TORRALVA M. Populational divergence in the impact of three nitrogenous compounds and their combination on larvae of the frog Pelophylax perezi (Seoane, 1885)[J]. Chemosphere, 2009, 76(7): 869-877.

[68] WOOD L, WELCH A M. Assessment of interactive effects of elevated salinity and three pesticides on life history and behavior of southern toad (Anaxyrus terrestris) tadpoles [J]. Environmental Toxicology and Chemistry, 2015, 34(3): 667-676.

[69] LIU R, QIN Y, DIAO J, et al. Xenopus laevis tadpoles exposed to metamifop: changes in growth, behavioral endpoints, neurotransmitters, antioxidant system and thyroid development[J]. Ecotoxicology and Environmental Safety, 2021, 220: 112417.

[70] SEMLITSCH R D. Adaptive genetic variation in growth and development of tadpoles of the hybridogenetic Rana esculenta complex[J]. Evolution, 1993, 47(6): 1805-1818.

[71] DENOËL M, D'HOOGHE B, FICETOLA G F, et al. Using sets of behavioral biomarkers to assess short-term effects of pesticide: a study case with endosulfan on frog tadpoles[J]. Ecotoxicology, 2012, 21: 1240-1250.

[72] HOLTSWARTH J N, ROWLAND F E, PUGLIS H J, et al. Effects of the neonicotinoid insecticide clothianidin on southern leopard frog (Rana sphenocephala) tadpole behavior[J]. Bulletin of Environmental Contamination and Toxicology, 2019, 103: 717-722.

[73] PREUD'HOMME V, MILLA S, GILLARDIN V, et al. Effects of

low dose endosulfan exposure on brain neurotransmitter levels in the African clawed frog Xenopus laevis[J]. Chemosphere, 2015, 120: 357-364.

[74] MIKó Z, UJSZEGI J, Gá L Z, et al. Effects of a glyphosate-based herbicide and predation threat on the behavior of agile frog tadpoles[J]. Ecotoxicology and Environmental Safety, 2017, 140: 96-102.

[75] LEE-JENKINS S S Y, ROBINSON S A. Effects of neonicotinoids on putative escape behavior of juvenile wood frogs (Lithobates sylvaticus) chronically exposed as tadpoles[J]. Environmental Toxicology and Chemistry, 2018, 37(12): 3115-3123.

[76] HAYES T B, KHOURY V, NARAYAN A, et al. Atrazine induces complete feminization and chemical castration in male African clawed frogs (Xenopus laevis)[J]. Proceedings of the National Academy of Sciences, 2010, 107(10): 4612-4617.

[77] FREITAS J S, GIROTTO L, GOULART B V, et al. Effects of 2, 4-D-based herbicide (DMA® 806) on sensitivity, respiration rates, energy reserves and behavior of tadpoles[J]. Ecotoxicology and Environmental Safety, 2019, 182: 109446.

[78] GDOVIN M J, JACKSON V V, ZAMORA D A, et al. Effect of prevention of lung inflation on metamorphosis and respiration in the developing bullfrog tadpole, Rana catesbeiana[J]. Journal of Experimental Zoology. Part A: Comparative Experimental Biology, 2006, 305(4): 335-347.

[79] LIGUORI I, RUSSO G, CURCIO F, et al. Oxidative stress, aging, and diseases[J]. Clinical Interventions in Aging, 2018, 13: 757-772.

[80] PIZZINO G, IRRERA N, CUCINOTTA M, et al. Oxidative stress: harms and benefits for human health[J]. Oxidative Medicine and Cellular Longevity, 2017, 2017: 1-13.

[81] 程宏毅, 郑善坚, 程福珍, 等. 六种农药对黑斑侧褶蛙的毒理效应[J]. 浙江师范大学学报(自然科学版), 2023, 46(2): 189-195.

[82] SCHUCH A P, MORENO N C, SCHUCH N J, et al. Sunlight damage to cellular DNA: Focus on oxidatively generated lesions [J]. Free Radical Biology and Medicine, 2017, 107: 110-124.

[83] SCHAVINSKI C R, DOS SANTOS M B, LONDERO J E L, et al. Effects of isolated and combined exposures of Boana curupi (Anura: Hylidae) tadpoles to environmental doses of trichlorfon and ultraviolet radiation[J]. Mutation Research/Genetic Toxicology and Environmental Mutagenesis, 2022, 883: 503549.

[84] BOCCIONI A P C, LENER G, PELUSO J, et al. Comparative assessment of individual and mixture chronic toxicity of glyphosate and glufosinate ammonium on amphibian tadpoles: a multibiomarker approach[J]. Chemosphere, 2022, 309: 136554.

[85] ZHANG J, QIAN L, WANG C, et al. UPLC-TOF-MS/MS metabolomics analysis of zebrafish metabolism by spirotetramat[J]. Environmental Pollution, 2020, 266: 115310.

[86] MENON J, ROZMAN R. Oxidative stress, tissue remodeling and regression during amphibian metamorphosis[J]. Comparative Biochemistry and Physiology. Part C: Toxicology & Pharmacology, 2007, 145(4): 625-631.

[87] WU Y Q, WANG C G, YUN W, et al. Antioxidant responses to benzo [a] pyrene, tributyltin and their mixture in the spleen of Sebasticus marmoratus[J]. Journal of Environmental Sciences, 2007, 19(9): 1129-1135.

[88] JIANG L, CHEN A, NIU F, et al. Antioxidant vitamin E protects embryos of Xenopus tropicalis against lambda-cyhalothrin induced embryotoxicity[J]. Environmental Science and Pollution Research, 2019, 26: 21629-21640.

[89] LIU X, WANG X, ZHANG F, et al. Toxic effects of fludioxonil on the growth, photosynthetic activity, oxidative stress, cell morphology, apoptosis, and metabolism of Chlorella vulgaris[J]. Science of the Total Environment, 2022, 838: 156069.

[90] 杨淑玉, 张蕊, 赵文阁, 等. 变态幼蛙对蝌蚪时期农药胁迫的毒性响应[J]. 生态学杂志, 2022, 41(3): 503-511.

[91] ZHANG W, DENG Y, CHEN L, et al. Effect of triadimefon and its metabolite on adult amphibians Xenopus laevis[J]. Chemosphere, 2020, 243: 125288.

[92] LIU T, WANG X, XU J, et al. Biochemical and genetic toxicity of dinotefuran on earthworms (Eisenia fetida)[J]. Chemosphere, 2017, 176: 156-164.

[93] 戴金妹, 张玲玲, 耿宝荣. 二硫氰基甲烷对斑腿泛树蛙蝌蚪抗氧化系统及丙二醛含量的影响[J]. 四川动物, 2016 (2): 283-287.

[94] 陈姣姣, 林玲, 郑金香, 等. 啶虫脒和噻虫嗪对镇海林蛙蝌蚪抗氧化活性的影响[J]. 福建师范大学学报(自然科学版), 2022, 38(2): 58-64.

[95] HALLIWELL B, GUTTERIDGE J M C. Free radicals in biology and medicine[M].Oxford: Oxford University Press, 2015.

[96] FERRARI A, LASCANO C, DE D'ANGELO A M P, et al. Effects of azinphos methyl and carbaryl on Rhinella arenarum larvae esterases and antioxidant enzymes[J]. Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology, 2011, 153(1): 34-39.

[97] PEUNOVA N, RAVI K, ENIKOLOPOV G, et al. No coordinates cell proliferation and morphogenetic cell movements during Xenopus early development[J]. Nitric Oxide-Biology and Chemistry, 2006, 14(4): A7-A7.

[98] TURHAN D O, GÜNGÖRD Ü A. Developmental, toxicological effects and recovery patterns in Xenopus laevis after exposure to penconazole-based fungicide during the metamorphosis process[J]. Chemosphere, 2022, 303: 135302.

[99] MASHA A, DINATALE S, ALLASIA S, et al. Role of the decreased nitric oxide bioavailability in the vascular complications of diabetes mellitus[J]. Current Pharmaceutical Biotechnology, 2011, 12(9): 1354-1363.

[100] BERNABò I, BIASONE P, MACIRELLA R, et al. Liver histology and ultrastructure of the Italian newt (Lissotriton italicus): normal structure and modifications after acute exposure to nonylphenol ethoxylates[J]. Experimental and Toxicologic Pathology, 2014, 66(9-10): 455-468.

[101] HAN W, TIAN Y, SHEN X. Human exposure to neonicotinoid

insecticides and the evaluation of their potential toxicity: an overview[J]. Chemosphere, 2018, 192: 59-65.

[102] ASCOLI-MORRETE T, BANDEIRA N M G, SIGNOR E, et al. Bioaccumulation of pesticides and genotoxicity in anurans from southern Brazil[J]. Environmental Science and Pollution Research, 2022, 29(30): 45549-45559.

[103] BERNABÒ I, GUARDIA A, MACIRELLA R, et al. Chronic exposures to fungicide pyrimethanil: multi-organ effects on Italian tree frog (Hyla intermedia)[J]. Scientific Reports, 2017, 7 (1): 6869.

[104] BERNABO I, GUARDIA A, MACIRELLA R, et al. Tissues injury and pathological changes in Hyla intermedia juveniles after chronic larval exposure to tebuconazole[J]. Ecotoxicology and Environmental Safety, 2020, 205: 111367.

[105] SAI L, QU B, LI Y, et al. Continued studies on the effects of simazine on the liver histological structure and metamorphosis in the developing Xenopus laevis[J]. Bulletin of Environmental Contamination and Toxicology, 2016, 97: 517-520.

[106] LI B, MA Y, ZHANG Y H. Oxidative stress and hepatotoxicity in the frog, Rana chensinensis, when exposed to low doses of trichlorfon[J]. Journal of Environmental Science and Health, Part B, 2017, 52(7): 476-482.

[107] ALNOAIMI F, DANE H, ŞIŞMAN T. Histopathologic and Genotoxic effects of deltamethrin on Marsh frog, Pelophylax ridibundus (Anura: Ranidae)[J]. Environmental Science and Pollution Research, 2021, 28: 3331-3343.

[108] CURI L M, PELTZER P M, ATTADEMO M A, et al. Alterations in gonads and liver tissue in two neotropical anuran species commonly occurring in rice fields crops[J]. Water, Air, & Soil Pollution, 2021, 232(5): 203.

[109] PAUNESCU A, PONEPAL C M, DRGHICI O, et al. Liver histopathologic alterations in the frog Rana (Pelophylax) ridibunda induce by the action of Reldan 40EC insecticide[J]. An Univ Oradea Fasc Biol, 2010, 17(1): 166-169.

[110] FRIEDMAN S L. The cellular basis of hepatic fibrosis—mechanisms and treatment strategies[J]. New England Journal of Medicine, 1993, 328(25): 1828-1835.

[111] SAAD E M, ELASSY N M, SALAH-ELDEIN A M. Effect of induced sublethal intoxication with neonicotinoid insecticides on Egyptian toads (Sclerophrys regularis)[J]. Environmental Science and Pollution Research, 2022, 29(4): 5762-5770.

[112] FENOGLIO C, ALBICINI F, MILANESI G, et al. Response of renal parenchyma and interstitium of Rana snk. esculenta to environmental pollution[J]. Ecotoxicology and Environmental Safety, 2011, 74(5): 1381-1390.

[113] PĂUNESCU A, PONEPAL C M, GRIGOREAN V T, et al. Histopathological changes in the liver and kidney tissues of marsh frog (Pelophylax ridibundus) induced by the action of Talstar 10EC insecticide[J]. Analele Universitatii din Oradea Fascicula Biologie, 2012, 19(1): 5-10.

[114] 马瑜, 李勃, 张育辉. 敌百虫对中国林蛙蝌蚪生长发育的毒性效应[J]. 生态毒理学报, 2014, 9(3): 531-537.

[115] ÇAKICI Ö. Histopathologic changes in liver and kidney tissues induced by carbaryl in Bufotes variabilis (Anura: Bufonidae) [J]. Experimental and Toxicologic Pathology, 2015, 67(3): 237-243.

[116] 姚丹. 敌敌畏和丁草胺对斑腿泛树蛙蝌蚪的毒性影响研究[D]. 福州: 福建师范大学, 2005.

[117] 陆娴婷, 赵美蓉, 刘维屏. 农药的免疫毒性研究[J]. 生态毒理学报, 2007(1): 10-17.

[118] 汪霞, 郜兴利, 何炳楠, 等. 拟除虫菊酯类农药的免疫毒性研究进展[J]. 农药学学报, 2017, 19(1): 1-8.

[119] BRODKIN M A, MADHOUN H, RAMESWARAN M, et al. Atrazine is an immune disruptor in adult northern leopard frogs (Rana pipiens)[J]. Environmental Toxicology and Chemistry: An International Journal, 2007, 26(1): 80-84.

[120] MARRON A O, AKAM M, WALKER G. Nitrile hydratase genes are present in multiple eukaryotic supergroups[J]. PLoS One, 2012, 7(4): e32867.

[121] CHRISTIN M S, MENARD L, GENDRON A D, et al. Effects of agricultural pesticides on the immune system of Xenopus laevis and Rana pipiens[J]. Aquatic toxicology, 2004, 67(1): 33-43.

[122] BEREZOVSKA O, FROSCH M, MCLEAN P, et al. The Alzheimer-related gene presenilin 1 facilitates notch 1 in primary mammalian neurons[J]. Molecular Brain Research, 1999, 69(2): 273-280.

[123] CELIK I, ISIK I, OZOK N, et al. Neurotoxic and immunotoxic effects of fenthion and omethoate on frogs at acute exposure[J]. Toxicology and Industrial Health, 2011, 27(4): 357-362.

[124] DAVIES M J, HAWKINS C L. The role of myeloperoxidase in biomolecule modification, chronic inflammation, and disease[J]. Antioxidants & Redox Signaling, 2020, 32(13): 957-981.

[125] LANGERVELD A J, CELESTINE R, ZAYA R, et al. Chronic exposure to high levels of atrazine alters expression of genes that regulate immune and growth-related functions in developing Xenopus laevis tadpoles[J]. Environmental Research, 2009, 109 (4): 379-389.

[126] MARTINI F, FERNáNDEZ C, SEGUNDO L S, et al. Assessment of potential immunotoxic effects caused by cypermethrin, fluoxetine, and thiabendazole using heat shock protein 70 and interleukin-1β mRNA expression in the anuran Xenopus laevis[J]. Environmental Toxicology and Chemistry, 2010, 29(11): 2536-2543.

[127] SIFKAROVSKI J, GRAYFER L, ANDINO F D J, et al. Negative effects of low dose atrazine exposure on the development of effective immunity to FV3 in Xenopus laevis[J]. Developmental & Comparative Immunology, 2014, 47(1): 52-58.

[128] ANDINO F D J, LAWRENCE B P, ROBERT J. Long term effects of carbaryl exposure on antiviral immune responses in Xenopus laevis[J]. Chemosphere, 2017, 170: 169-175.

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