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从欧洲视角探究食物中天然毒素对健康的潜在长期风险（中英文）

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摘　要：食品中完全无毒素的理念往往更接近于一种理想化的幻想而非现实。为辨别并优先处理长期摄入食品累积的有害物质，特别是天然毒素带来的健康风险，我们开展了一项针对性研究。通过审查 100 多项主要由欧洲食品安全局（EFSA）开展的欧洲层面的风险评估研究来评估食品供应的安全性。深入探讨了欧洲消费者长期接触的食品中潜在天然毒素对健康的影响，以及关于特定毒素的研究发现。此外，尝试对长期接触与公众健康有关的食品化学污染物所构成的风险进行排名。黄曲霉毒素被列为食品中第三大重要的化学污染物，因其具有很强的致癌能力，会导致人类患肝癌，加之欧洲谷物类食品消费量高，导致了高风险。虽然吡咯碱类物质具有基因毒性和致癌性，但由于人类接触这类植物毒素的来源有限——例如通过茶、蜂蜜或草药，它们在榜单中仅排第五。

关键词：欧洲视角；天然毒素；食品供应；安全性；风险评估

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Chronical Health Risks from Natural Toxins in Our Food – From a European Perspective(Chinese and English versions)

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Abstract: The notion of toxin-free food may be more of a fantasy than a factual reality. To help identify and prioritize health risks associated with long-term consumption of harmful substances and especially of natural toxins through food, a dedicated study was conducted. We assessed the safety of our food supply by examining over 100 risk evaluations carried out at the European level, primarily by the European Food Safety Authority (EFSA). We analysed in depth the potentially hazardous natural toxins in food that European consumers are chronically exposed to. In this review, the health implications of these contaminants, their potential risk for average consumers in Europe and the findings from our study regarding individual toxins are discussed. We have also made an attempt to rank the risks posed through chronical exposure to chemical food contaminants that are of concern for public health. Aflatoxins are ranked as the third most important chemical contaminant in our food since they pose a high risk due to their significant carcinogenic potency causing liver cancer in humans coupled with the high consumption of cereal-based foods in Europe. Despite their genotoxic and carcinogenic effects, pyrrolizidine alkaloids occupy only the fifth position due to their limited sources – tea, honey, or herbs – of human exposure to this group of plant toxins.

Key words: a European perspective; natural toxins; food supply; safety; risk evaluations

即使在欧洲这样的先进地区，消费者也经常会暴露于污染食品供应链的复杂有害物质混合物中（包括致癌物），可能带来潜在的长期健康威胁[1]。尽管这些污染物较为隐蔽，但可以追溯到从自然发生到工业过程的各种来源。例如黄曲霉毒素 B1，自然存在于花生和谷物中，作为一种强效的基因毒性致癌物，主要由曲霉菌（Aspergillus flavus）产生，并能对 DNA 和蛋白质造成严重损害[2]。

然而，值得注意的是这些污染物的来源并不总是被准确认识。例如，在 11 世纪，爆发了一起可引发所谓的“圣火症”的食物污染事件，导致受害者发生严重的肢体腐烂及其他衰弱体质的健康问题。由于认知有限，人们将这起食物污染事件归因于巫术[3]。后来，人们发现这些症状实际应归因于麦角菌——一种在 17 世纪污染了黑麦面粉的真菌。“圣火症”的临床表现是由 Claviceps purpurea 霉菌产生的有毒化合物麦角类生物碱引起的。

麦角类生物碱以其复杂的化学结构和迅速转化为其对映异构体的特性而闻名。这些结构变化对精准定量检测带来极大挑战性。摄入这类毒素可能引起一系列症状，包括血管收缩、幻觉、癫痫发作，甚至死亡[4]。17 世纪，由于麦角碱的精神活性作用，摄入受污染的麦角面粉引发了“圣火症”（麦角病）的大规模爆发，这场疫情导致了大规模的恐慌和暴力行为。

随着研究的深入，科学家发现麦角碱不仅存在于黑麦面粉中，还广泛分布于其他食品，如小麦、大麦、燕麦，甚至啤酒等。这些普遍存在食品供应链中的污染物仍是一个严峻的问题，因为它们持续对公共健康构成潜在威胁。此外，麦角碱及其对映异构体的复杂性需要先进的分析技术手段来准确定量检测分析[3]。

另一个自然发生的食品污染物的例子是由镰刀菌产生的真菌毒素，包括脱氧雪腐镰刀菌毒素和玉米赤霉烯酮。这些真菌毒素已被证实与一系列健康问题相关联，包括免疫系统抑制、生殖功能障碍，乃至癌症。真菌毒素可以污染多种农作物，包括小麦、玉米和稻米，迫使食品生产商必须采取严格的监测和防控措施，以减少这些毒素对食品供应链的污染。

工业生产也可能引入食品污染物[1]。例如，现代农业生产中农药和其他农业化学品的使用可能会导致其残留，当人体大量摄入时可能会造成健康风险。此外，持久性有机污染物等工业副产品可以通过畜牧业使用受污染的饲料等各种途径进入我们的食品供应链[5]。

这些污染物的存在凸显了对食品供应链进行严格监控和管理的紧迫性，以最大限度地降低潜在的健康风险。分析化学家通过开发和实施先进的分析技术，识别检测、定量分析和减少食品污染物对公众健康的影响发挥着至关重要的作用。通过深入了解这一领域的最新研究和发展，分析化学家、毒理学家和食品科学家正密切合作，以确保我们及子孙后代的食品供应安全可靠。

1 （分析）化学

现代分析化学，凭借其先进且高灵敏度的技术，已成为保障食品安全的关键工具。尽管这些技术能够检测到极微量的污染物，如十亿分之一（ppb）级别的浓度，但也有批评声音认为，这种高灵敏检测可能导致对新兴食品危机的过度担忧。像《无毒食品？》[1]这本书的作者一样，分析化学家们将他们的职业生涯致力于识别我们食品供应中不断增加的污染物种类。

尽管存在争议，但承认综合分析方法在确保食品安全方面扮演的核心角色是至关重要的。准确检测和量化食品产品中的污染物是进行系统风险评估和维护公共健康的先决条件。采用最先进的分析技术，如新一代质谱仪的引入，使得能够同时确定食品和饲料样品中数百种物质的含量成为可能。这些强大但高成本的技术对于保障我们食品供应的安全至关重要。在奥地利维也纳附近图尔恩的维也纳自然资源与生命科学（BOKU）大学的科学家们创造性地开发了一种独特的分析方法，这种方法能够在短短 45 min 内同时定量分析超过 1 200 种污染物，包括 300 多种真菌毒素、50 种植物毒素、150 种兽药和 500 种农药[6-7]。

尽管我们在使用复杂的分析方法检测污染物方面取得了显著的进展，但在理解这些污染物的毒理学意义上仍存在显著的差距。毒理学特征涉及确定这些物质在人体中的毒性效应、吸收、分布和代谢方式。困难的是，为了准确评估这些污染物可能带来的风险，需要进行广泛的测试，例如细胞培养，通常还涉及动物试验。

值得注意的是，尽管我们在食品安全的分析方法方面取得了进步，但对于许多潜在污染物的毒理学影响和意义，目前的了解仍然非常有限。深入理解这些污染物对公共健康的可能影响，要求持续地进行研究，开发出更加精确、高效的分析工具。

2 真菌毒素的风险

天然毒素或生物毒素由各种生物生产，从简单的分子到复杂的化合物不等。在农业领域中，真菌毒素代表了一类关键的天然毒素，这些毒素源自于真菌，并于作物在田间生长或在不适宜的储藏条件下形成[1]。据估计，全球各种生态系统中存在数百万种真菌，其中近 15 万种真菌[8]已被鉴定，它们能够产生超过 20 万种不同的次级代谢物，其中超过 300 种被鉴定为真菌毒素。根据现有知识，约有 50 种真菌毒素在食品和饲料中较为常见，它们的浓度水平各不相同。

在正常条件下，植物和真菌主要产生氨基酸、碳水化合物和脂肪等必需物质。当受到环境压力或缺乏营养时，植物和真菌都会转向次级代谢。在作物开花旺盛时期，植物的抗性通常会增强。因此，诸如镰刀菌、曲霉或青霉等真菌在从受感染的宿主（作物）中获取足够营养方面面临困难，这种压力状态促使真菌转向产生真菌毒素及其他化合物的次生代谢途径。这些毒素的主要作用是为了保护真菌种类或通过损害宿主植物的健康来减弱其生存能力，其对人体和动物具有恶心、呕

吐、体重下降、不育症到肝癌等一系列不良健康影响。此外，真菌毒素还在农业中造成了重大经济损失。据估计，仅在欧洲，每年因真菌毒素的作物减产和相关动物健康问题造成的经济损失高达 15 亿欧元[9]。

2.1 黄曲霉毒素

真菌毒素之所以臭名昭著主要是因为黄曲霉菌产生的黄曲霉毒素，在气候较温暖的地区，包括欧洲南部的作物中占主导地位。黄曲霉毒素成为食品工业关注的焦点始于 20 世纪 60 年代初，当时英格兰有超过 10 万只幼年火鸡在食用受污染的巴西花生饲料后死亡[10]。随后的调查明确了黄曲霉毒素的危害，其名称源自其主要产毒者黄曲霉菌。自那时起，发现了多种类型的黄曲霉毒素，其中黄曲霉毒素 B1 因其强致突变和致癌性等强毒性和农业的相关性而备受关注。黄曲霉毒素 B1 主要存在于坚果、干果和谷物中。与前面提到的镰刀菌毒素不同，黄曲霉毒素 B1 在摄入后会在肝脏被代谢为更活跃的分子，该分子直接与 DNA 中的鸟嘌呤碱基结合，通过基因毒性机制导致潜在的癌症形成[11]。人们认为，这一过程没有安全阈值剂量，这意味着即便极少量的摄入也可能致癌。此外，长期低水平暴露于黄曲霉毒素与人类肝癌存在关联。国际癌症研究机构已将黄曲霉毒素归类为“对人类致癌”（第一组）[12]，虽然在欧洲黄曲霉毒素在肝癌发展中的作用被视为有限，但即使摄入黄曲霉毒素含量在法定限量范围内的食品，仍对普通欧洲消费者构成潜在的健康风险，预计随着全球气候变暖[2,13]，这种风险将进一步增加[14]。

2.2 镰刀菌毒素

除黄曲霉毒素外，欧洲饮食中主要遇到的另一组重要真菌毒素是由镰刀菌产生的。在欧洲温和的气候条件下，这些真菌可能会污染谷物——构成欧洲最重要的饮食组成部分，并产生几种毒素，这包括脱氧雪腐镰刀菌烯醇（因其高暴露水平导致呕吐而被称为呕吐毒素）、T-2 毒素、HT-2 毒素、玉米赤霉烯酮和伏马菌素。还有所谓的隐蔽型真菌毒素，这些毒素能够通过植物的甘露糖化作用与葡萄糖分子结合，从而被植物解毒[15]。脱氧雪腐镰刀菌素与动物体重减少以及免疫功能受损有关，即使在低剂量下也有大量的研究支持这一点[15]。同样，T-2 和 HT-2 毒素同样显示出免疫功能受损的效应[16]。玉米赤霉烯酮及其代谢物是一类具有独特性的真菌毒素，作为内分泌干扰物影响机体。这些物质即使在微剂量下也可能通过扰乱激素系统而导致伤害，并可能引起动物的不育问题。

根据欧洲食品安全局[15]的评估，长期饮食暴露于脱氧雪腐镰刀菌素及其类似物对欧洲成年普通消费者来说并不构成健康风险，然而，年轻消费者可能面临潜在的健康风险。同样地，在欧洲，与 T-2 毒素、HT-2 毒素、玉米赤霉烯酮和伏马菌素相关的健康问题较少见，这些问题主要通过以玉米为基础的食品引起[17-19]。由于真菌毒素在热处理过程中稳定，即使经过烘焙也能保持其毒性，因此，严格的谷物收获筛选和清洁操作是降低这些毒素风险的关键措施。

2.3 赭曲霉毒素 A

赭曲霉毒素 A 是欧洲常见的真菌毒素，这种毒素来源于青霉和曲霉属。欧洲人主要通过食用保存的肉类、奶酪、谷物及其制品、干果、新鲜水果以及果汁等食物接触到赭曲霉毒素 A[20]。国际癌症研究机构（IARC）将赭曲霉毒素 A 归类为“可能对人类致癌”（2B 类）。摄入赭曲霉毒素 A 可能通过遗传毒性和非遗传毒性机制导致肾癌。如果最终确定是遗传毒性直接引起的，那么欧洲消费者由于长期饮食暴露于这种真菌毒素而面临潜在的健康风险[21]。然而，目前的研究表明健康问题较低[22]，因此，暂时认为赭曲霉毒素 A 的慢性饮食暴露对欧洲成年普通消费者不构成潜在风险[21]。人类炎症性肾病与膳食赭曲霉毒素 A 暴露之间的因果关系尚不确定[20]。

交联孢霉菌属（Alternaria）的真菌在高温和高湿环境下更容易生长，气候变化使它们在中欧地区风险越来越高。交联孢霉菌属主要导致植物疾病，可通过灰褐色斑点识别，但也会形成有毒物质[20]。这些毒素中的一些具有遗传毒性潜力，但目前缺乏足够的证据对其进行 IARC 分类[23]。因

此，长期暴露于交联孢霉菌属毒素和麦角毒素、脱氧雪腐镰刀菌素、雪腐镰刀菌素和串珠镰刀菌素对欧洲各年龄段的消费者并没有造成重大风险[20]。串珠镰刀菌素由于其微小的分子，在各年龄段的普通欧洲消费者中都只构成轻微的健康问题[24]。

2.4 新兴真菌毒素

食品中存在一些较不常见的真菌毒素，这些毒素通常以较低的浓度出现。随着先进分析技术的发展，新类型的真菌毒素被识别出来，包括所谓的隐蔽型真菌毒素和一些独特性的毒素，如恩镰孢菌素。这些化合物增加了欧洲消费者对真菌毒素的总体暴露。然而，由于缺乏足够的数据，目前还无法进行可靠的风险评估。其他所谓的新兴真菌毒素，如杂色曲霉素和桔青霉素，也受到关注。杂色曲霉素与黄曲霉毒素共享生物合成路径，在动物研究中显示出了致癌潜力[20]。桔青霉素也表现出致癌性质，尽管它们在欧洲食品中的出现率很低，暗示膳食暴露水平很小，但关于白僵菌素和恩镰孢菌素的毒理学信息仍然模糊不清。白僵菌素和恩镰孢菌素作为离子载体，能够跨越生物膜传输钾离子。尽管现有的风险评估数据并不十分完整，但它们在食品中的频繁检出意味着普通欧洲消费者可能面临潜在的健康风险[24]。

3 植物次生代谢产物

植物次生代谢产物是植物为了抵御天敌、疾病或环境压力而自然产生的物质。这些化合物可能污染食品和饲料产品，对各个年龄段和饮食习惯的消费者构成潜在风险[1]。

3.1 吡咯啉生物碱

防风草（Senecio serradalis）是诸多能够产生所谓的保护性化合物——吡咯啉生物碱的植物之一。这些化合物通过使植物变得不可口或不可食用来阻止天敌，如毛毛虫和人类。虽然在大约 600 种已知的吡咯啉生物碱中，只有约 30 种对食品和饲料安全构成显著威胁，但高浓度的污染有可能引发人体急性肝中毒，甚至可能导致死亡。然而，对欧洲消费者来说，目前这种潜在风险较低[25]。国际癌症研究机构（IARC）将某些吡咯啉生物碱归类为“可能对人类致癌”（第 2B 组）的物质。

3.2 曲普碱

在众多植物种类中存在着超过 200 种不同的曲普碱，包括曼陀罗等在谷物田中生长的植物。在收获过程中，有些有害的植物种子及其含有的生物碱化合物，可能会混入谷物产品中。一些曲普碱已经受到了广泛的科学关注，尽管它们是一些如土豆等食品作物产生的。人类对这些生物碱的急性暴露可能会引起神经系统问题。目前，由于数据的不足，只对幼儿的饮食暴露进行了评估，并表明存在潜在风险[26]。然而，根据最近的欧洲范围内调查，多种曲普碱存在于各种食品中，其中一些含量较高[27]。这表明其他消费群体也可能面临潜在风险。

3.3 芥酸

芥酸是一种天然存在的成分，在菜籽油和芥末等十字花科植物中含量较高。化学结构上，芥酸是一种长链的单不饱和 ω-9 脂肪酸。虽然过度接触芥酸可能会对人体健康产生负面影响，导致脂肪性心脏病，但据欧洲食品安全局[28-29]的评估，对于欧洲各年龄段的普通消费者而言，芥酸并不构成潜在风险。

3.4 氰甙

氰甙是一类多样化的天然毒素，每种都含有一个醇（糖）分子和一个碳水化合物（碳水化合物）分子，以及一个氰基。在这种状态下，化合物保持非毒性。在酶降解过程中，它释放出有毒的氢氰酸（HCN），也称为氰化氢。这一过程首先涉及一种酶将糖单元（通常是葡萄糖）分解，释放氢氰酸。杏仁甙，存在于苦杏仁和杏仁核中，是这一类物质的一个著名例子。生杏仁被咀嚼或研磨时，氰甙会释放出氢氰酸。对幼儿而言，即使一颗小的杏仁核也可能产生健康风险，而成人则可以安全食用三颗小的或不到一半的大杏仁。人类对氢氰酸的暴露可能引起严重的急性毒性反应，甚至死亡。尽管如此，目前对氰化物的慢性毒性的数据有限，尚未确定欧洲消费者是否存在潜在风险[20]。

4 海洋生物毒素

海洋生物毒素是一种对海洋生物与人类健

康均构成隐形却显著性风险的物质。全球的海洋和海域中约存在 5 000 种藻类，其中大约有 300 种能够大面积繁殖，导致大型水域出现褐潮等现象[1]。部分藻类在大量繁殖时会产生有毒的次生代谢物——海洋生物毒素。这些毒素会在贝类和其他滤食动物的组织中积累，这些生物通过摄食藻类而间接摄入毒素，进而也可能累积在鱼类和其他海产品中。

海洋生物毒素具有高药效性，人体一旦摄入可能会引发从轻微的嘴唇周围刺痛或麻木到死亡的急性症状。为确保公众安全，贝类养殖区和贝类产品在向消费者销售前，会定期进行海洋生物毒素的污染检测。然而，这些毒素的含量可能因季节性和年度气候条件而变化，导致人们的膳食暴露水平及其相关的健康风险出现不一致。

在欧洲水域，萨克西毒素、岩藻酸和海藻酸是最常见的海洋生物毒素。目前由于数据不足，对于普通海鲜消费者的慢性健康风险评估尚不明确。然而，大量摄食贝类的人可能面临潜在危害，这是因为欧盟的最大限量值可能并不总是提供充分的保护措施。此外，一些海洋生物毒素在欧盟没有法定限量，但这些毒素的出现频率可能会随着气候变化而改变。

烹饪方法如热加工可以影响贝类中的毒素水平，这可能会导致毒素水平的增加或减少[30]。此外，在地表水和海洋环境中发现的蓝藻细菌也可以产生氰毒素，这可能会污染饮用水和食品。然而，欧洲人群对于这些毒素的暴露水平尚未确定[31]。随着来自亚洲的水产养殖产品在市场上的日益流行，由于消费量的增加，可能会导致人群对这类毒素的显著暴露增加。

5 风险排名和结论

本文专注于将已识别的污染物根据它们引起的不同类型的有害效应以及通过饮食摄入的日常量进行分类和排序，旨在评估其潜在慢性风险。值得注意的是，本文的排名仅包括由欧洲食品安全局（EFSA）确认为对成年人构成慢性风险的污染物，而那些被认为风险较低的污染物则被排除在外[1]。这一慢性化学食品安全风险的排序并没有考虑到 EFSA 风险评估中存在的不确定性因素，例如缺失的毒理学或暴露数据。因此，这种风险排序应被视为一种指示性的工具。

首先，食品加工过程中产生的污染物被认为具有最高的潜在慢性风险，这是由于它们的遗传毒性和致癌性，尽管这些效应在人类中尚未得到明确证实，但这些污染物在日常食品中广泛存在，使得它们的风险问题更加凸显。其次是多环芳烃类，这些污染物同样因其遗传毒性和致癌性而备受关注，尽管缺乏直接的人类研究证据[1]。这类污染物在多种食品中普遍存在。

排在本文列表第三位的是黄曲霉毒素，这种毒素因其在人体内引发肝癌的显著致癌性而被视为高风险。鉴于欧洲人群大量消费谷基食品，这使得谷物成为这些污染物的主要暴露源。尽管如此，更常受到黄曲霉毒素污染的坚果和玉米在欧洲的消费量相对较低。

本文排名第四的污染物包括二恶英、类二恶英多氯联苯、镍以及一种溴系阻燃剂，它们之所以排名如此之高，是因为这些物质在许多日常消费的食品中普遍存在。尽管这一组植物毒素具有遗传毒性和致癌性，但因为人类暴露的来源相对有限。吡咯嗪生物碱排名第五 – 这类毒素主要存在于茶、蜂蜜或草药中[1,20]。

需要特别指出的是，人们通过日常饮食摄入的潜在毒素混合物对健康的慢性影响尚不明确。值得注意的是，上述几种污染物由于具有遗传毒性和致癌性它们的联合暴露可能增加健康风险，这种风险可能超出了对单个化学物质进行评估时的预期[20]。

6 结论（针对欧洲消费者）

总之，欧洲消费者受益于国家和欧洲层面的严格食品安全法规，确保食品供应比以往任何时期都更安全。然而，即便如此，必须接受一个事实：在我们的食物中完全消除毒素是一个无法实现的目标。现代分析技术的进步使得检测、鉴定和量化愈来愈小浓度的污染物成为可能，这要求监管机构不断更新其标准和并调整其指南。

一个值得关注的新兴领域是关于化学污染物

混合物暴露的健康风险，即所谓的“毒性鸡尾酒”效应。这些化学物质混合物可以复杂的方式相互作用，可能导致加和甚至是协同效应，从而带来的健康风险可能超过了针对单个化学物质评估的风险。例如，一些污染物可以作为内分泌干扰物，改变激素平衡并增加人体对其他毒素的敏感性。

食品污染的潜在健康风险因气候变化而进一步加剧。气候变暖、降水模式的改变以及极端天气事件的增加可能会影响农业生产，并进一步促进了食物中有毒化合物的积累。此外，有研究报道称，病原微生物和植物害虫正以每年 3~5 km 的速度向极地扩散[32]，这可能导致即使在中欧也出现前所未有的高水平的黄曲霉毒素污染。

预计未来欧盟的风险管理措施将进一步减少欧洲消费者通过饮食摄入化学污染物的风险[33]。例如，欧洲食品安全局（EFSA）定期根据新的科学数据和对其健康风险的不断发展的认识更新其对污染物的指导值。此外，监管机构正在不断努力改善农业生产，减少对有害农药的依赖，并推广更环保的生产方式，最小化食品中的污染物积累。

总之，尽管欧洲消费者可以放心地依赖全面的食品安全法规，但仍需要对食品中化学污染物的潜在健康风险保持警惕。通过关注均衡饮食，优先选择天然食物，并限制过度加工食品的摄入，消费者可以在最大程度上减少对这些污染物的暴露，同时促进整体健康和福祉。此外，监管机构在提高食品安全标准和减少污染物积累方面的持续努力，将有助于为子孙后代提供更健康、更安全的食品供应。

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Chronical Health Risks from Natural Toxins in Our Food – From a European Perspective (英文原文)

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Abstract: The notion of toxin-free food may be more of a fantasy than a factual reality. To help identify and prioritize health risks associated with long-term consumption of harmful substances and especially of natural toxins through food, a dedicated study was conducted. We assessed the safety of our food supply by examining over 100 risk evaluations carried out at the European level, primarily by the European Food Safety Authority (EFSA). We analysed in depth the potentially hazardous natural toxins in food that European consumers are chronically exposed to. In this review, the health implications of these contaminants, their potential risk for average consumers in Europe and the findings from our study regarding individual toxins are discussed. We have also made an attempt to rank the risks posed through chronical exposure to chemical food contaminants that are of concern for public health. Aflatoxins are ranked as the third most important chemical contaminant in our food since they pose a high risk due to their significant carcinogenic potency causing liver cancer in humans coupled with the high consumption of cereal-based foods in Europe. Despite their genotoxic and carcinogenic effects, pyrrolizidine alkaloids occupy only the fifth position due to their limited sources – tea, honey, or herbs – of human exposure to this group of plant toxins.

Key words: a European perspective; natural toxins; food supply; safety; risk evaluations

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1 INTRODUCTION

Even in sophisticated regions like Europe, consumers are frequently exposed to complex mixtures of hazardous substances that infiltrate our food supply, posing potential long-term health risks, including cancer-promoting agents (carcinogens) [1]. These contaminants, though often hidden from view, can be traced back to various sources, ranging from natural occurrences to industrial processes. One well-known example of this is aflatoxin B1, which is naturally found in peanuts and cereals. This potent genotoxic carcinogen is mainly produced by *Aspergillus flavus* fungus and can cause severe damage to DNA and proteins[2].

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However, it is essential to recognize that the sources of these contaminants are not always as clear-cut as they once were. In the 11th century, for instance, witches were blamed for food contamination outbreaks leading to symptoms known as Holy Fire, which resulted in severe limb rot and other debilitating health effects[3]. These incidents were later attributed to ergot, a fungus that contaminated rye flour in the 17th century. The symptoms of Holy Fire were caused by ergot alkaloids, a group of toxic compounds produced by the *Claviceps purpurea* fungus.

Ergot alkaloids are characterized by their complex chemical structures and ability to transform rapidly into their mirror images, referred to as epimers. These structural modifications make them challenging for analytical chemists to detect and quantify accurately. Consumption of these toxins can lead to a range of symptoms, including vasoconstriction, hallucinations, seizures, and even death[4]. Ingestion of ergot-contaminated rye flour during the 17th century led to widespread outbreaks of St. Anthony's Fire (ergotism), resulting in mass hysteria and violent behaviours due to the psychoactive effects of these alkaloids.

As research progressed, scientists discovered that ergot alkaloids were not unique to rye flour but could be found in various other foods, including wheat, barley, oats, and even beer. The presence of these contaminants in our food supply remains a significant concern today, as they continue to pose potential health risks. Moreover, the complexity of ergot alkaloids and their epimers necessitates advanced analytical techniques for detection and quantification[3].

Another example of naturally occurring food contaminants is mycotoxins produced by the Fusarium fungus. These toxins include deoxynivalenol and zearalenone, which have been linked to various health issues such as immunosuppression, reproductive disorders, and even cancer. Mycotoxins can contaminate a wide range of crops, including wheat, corn, and rice, making it essential for food manufacturers to implement rigorous monitoring and mitigation strategies to minimize the presence of these toxins in our food supply.

Industrial processes can also contribute to the presence of food contaminants[1]. For instance, the use of pesticides and other agrochemicals in modern farming practices can lead to residues that may pose health risks when consumed in large quantities. Additionally, industrial by products such as persistent organic pollutants can find their way into our food supply through various means, including the use of contaminated feed for livestock[5].

The presence of these contaminants highlights the importance of rigorous monitoring and regulation of our food supply to minimize potential health risks. Analytical chemists play a crucial role in this process by developing and implementing advanced analytical techniques to detect, quantify, and mitigate the impact of food contaminants on public health. By staying informed about the latest research and developments in this field, analytical chemists, toxicologist and food scientists shall continue to working together to ensure the safety and integrity of our food supply for generations to come.

2 (ANALYTICAL) CHEMISTRY

Modern analytical chemistry, driven by advanced and sensitive techniques, has become a double-edged sword for food safety. While these methods enable the detection of increasingly smaller quantities of contaminants, such as parts per billion (ppb), some critics argue that they could also be considered a source of emerging food crises. Analytical chemists, like the authors of the book “Toxin-Free Food?”[1] have dedicated their careers to identifying an expanding array of substances in our food supply.

However, it is crucial to acknowledge the role of comprehensive analytical methods in ensuring food safety. The ability to accurately detect and quantify contaminants in food products is a prerequisite for conducting thorough risk assessments and safeguarding public health. State-of-the-art analytical methods, such as the introduction of new generation mass spectrometers, enable the simultaneous determination of concentrations for hundreds of substances in food and feed samples. This powerful yet expensive approach is essential for conducting comprehensive risk assessments for potentially harmful contaminants in our food supply. At BOKU University in Tulln near Vienna in Austria, scientists have pioneered a unique method capable of quantifying more than 1,200 contaminants simultaneously, including over 300 mycotoxins, 50 plant toxins, 150 veterinary drugs, and 500 pesticides, within 45 minutes per sample[6-7].

While we have made considerable progress in detecting contaminants using sophisticated analytical methodologies, there remains a significant gap in our understanding of their toxicological relevance. Toxicological characterisation involves determining the toxic effects, absorption, distribution, and metabolism of these substances in humans. Unfortunately, extensive testing, such as on cell cultures but also often still involving animals, is required to accurately assess the potential risks posed by these contaminants.

It is worth noting that despite our advancements in analytical methods for food safety, we still have limited knowledge about the toxicological significance of many potential pollutants. Understanding their impact on public health requires continued research efforts and the development of more precise and less time-consuming analytical tools.

3 RISKS FROM FUNGAL TOXINS (MYCOTOXINS)

Natural toxins or biotoxins are produced by various living organisms, ranging from simple molecules to complex chemical compounds. In agriculture, mycotoxins are a significant class of natural toxins that originate from fungi. Mycotoxins are toxic secondary metabolites formed when fungi inhabit crops in the field or during improper storage conditions[1]. Estimates suggest that there are several million species of fungi existing in various ecosystems of Earth, of which nearly 150,000 species of fungi[8] have been described, which can easily produce more than 200,000 distinct secondary metabolites, with over 300 identified as mycotoxins. Some 50 of which are commonly found in food and feed at various concentration levels based on current knowledge.

Under normal conditions, plants and fungi primarily generate essential substances like amino acids, carbohydrates, and fats. When confronted with environmental stressors or a lack of nutrients, both plants and fungi switch to secondary metabolism. During the crop's full blooming phase, plants exhibit increased resistance. Consequently, fungal species such as Fusarium, Aspergillus, or Penicillium face difficulty in obtaining sufficient nutrients from their infected host (the crop). Stressed conditions result in the fungi switching to secondary metabolism, leading them to produce mycotoxins and other chemical compounds. The primary purpose of these 'toxin arrows' is to protect the fungal species or weaken their hosts (plants) by damaging their health. This adversely impacts human and livestock health. Mycotoxins exhibit a wide range of adverse effects, ranging from nausea, vomiting, weight loss, infertility, and liver cancer. Moreover, they cause substantial economic losses in agriculture. According to expert estimates, annual crop loss and related consequences for animal health, primarily in Europe, cost approximately €1.5 billion[9].

3.1 Aflatoxins

The notoriety of mycotoxins is largely attributed to aflatoxins, produced by Aspergillus fungi predominantly in crops grown in warmer climatic regions of the world including Europe's south. Their emergence as a significant concern in the food industry can be traced back to the early 1960ies when over 100,000 young turkeys in England succumbed after consuming contaminated Brazilian peanut meal[10]. The subsequent investigation identified aflatoxins, which derive their name from *Aspergillus flavus*, their primary producer. Among various aflatoxins discovered since, aflatoxin B1 stands out for its toxicological and agricultural relevance due to its potent mutagenic and carcinogenic properties. Aflatoxin B1is primarily found in nuts, dried fruits, and cereals. Unlike the Fusarium toxins mentioned earlier, when ingested, the liver metabolizes aflatoxin B1 into a more reactive molecule that binds directly to DNA at the guanine base, leading to potential cancer formation through genotoxic mechanisms[11]. It is believed that there is no threshold dose for this process, implying even small amounts can be carcinogenic. Also, chronic low-level exposure to aflatoxins is linked to liver cancer in humans. Aflatoxins are classified as "carcinogenic to humans" (Group 1) by the International Agency for Research on Cancer[12] and aflatoxins, despite their limited role in Europe's liver cancer development, remain a potential health risk for average European consumers even when legal limits for their presence in food are adhered[2,13] which is expected to increase as a result of global warming [14].

3.2 Fusarium Toxin

Apart from aflatoxins, European diets primarily encounter Fusarium-derived mycotoxins. In Europe's generally temperate climate conditions, these fungi may contaminate cereals – the most important dietary source for European - and produce several toxins, namely deoxynivalenol (vomitoxin due to its high exposure level causing vomiting), T-2 toxin, HT-2 toxin, zearalenone, and fumonisins. Masked mycotoxins also exist, originating from crops that can detoxify these toxins by binding them to a glucose molecule through glycosylation[15]. Deoxynivalenol is linked to reduced weight gain in animals and immunological impairment even at low doses, as evident from numerous studies[15]. Similarly, T-2 and HT-2 toxins exhibit immunocompromising effects[16]. Zearalenone and its metabolites represent a distinct class of fungal toxins, acting as endocrine disruptors. These substances can cause harm even at minimal doses by altering the hormonal system and leading to infertility in farm animals.

Chronic dietary exposure to deoxynivalenol and its analogues do not pose a health risk to average adult European consumers in Europe, while young consumers are at potential risk[15]. Similarly, minimal health concerns arise from T-2 toxin, HT-2 toxin, zearalenone, and fumonisins, primarily through corn-based foods in Europe[17-19]. Thermally stable, mycotoxins maintain their potency even during baking, necessitating rigorous harvested grain selection and cleaning to mitigate their presence.

3.3 Ochratoxin A

Ochratoxin A is a mycotoxin commonly encountered by Europeans. This toxin derives from the genera Penicillium and Aspergillus. Major sources of ochratoxin A exposure in Europe include preserved meat, cheese, grains, grain-based products, dried and fresh fruits, and fruit juices[20]. IARC has classified ochratoxin A as “possibly carcinogenic to humans” (Group 2B). Both genotoxic and non-genotoxic mechanisms can potentially contribute to kidney carcinogenesis upon ochratoxin A intake. If it is ultimately determined that genotoxicity is direct, then European consumers face a potential health risk due to the long-term dietary exposure to this mycotoxin[21]. However, this is still under investigation, implying currently low health concerns[22]. Hence, the current chronic dietary exposure to ochratoxin A is not a potential risk for the average adult European consumers[21]. The causal relationship between human inflammatory kidney disease and dietary OTA exposure remains speculative[20].

Fungal sources of *Alternaria* preferably thrive at high temperatures and humidity, making them increasingly relevant to Central Europe due to climate change. *Alternaria* primarily causes plant diseases recognizable by grey-brown spots, but it also forms toxic substances[20]. Some of these substances exhibit genotoxic potential, yet insufficient evidence exists for IARC classification[23]. Therefore, chronic dietary exposure to *Alternaria* toxins and ergot alkaloids, deoxynivalenol, nivalenol, and moniliformin poses no significant risk to European consumers of any age[20]. Moniliformin, with its tiny mycotoxin molecule, represents a minor health concern for average European consumers at any age[24].

3.4 Prevalent mycotoxins

Several less prevalent mycotoxins exist in food at generally low concentrations, as mentioned above. Advanced analytical techniques have led to the identification of new mycotoxins, including masked mycotoxins and “exotic” types like enniatins. These compounds expand the overall mycotoxin exposure for European consumers. However, due to limited data availability, it is currently impossible to perform a reliable risk assessment. Some other examples of such so-called emerging mycotoxins include sterigmatocystin and citrinin. Sterigmatocystin shares a biosynthetic pathway with aflatoxins and has been found to be carcinogenic in animal studies[20]. Citrinin also exhibits carcinogenic properties. Although their occurrence in European foods is low, suggesting minimal dietary exposure, ambiguous data exist regarding the toxicity of beauvericin and enniatins. Beauvericin and enniatins are ionophores, which means they can transport potassium ions across biological membranes. While existing risk assessments are not highly robust, their frequent occurrence in foods implies a potential health risk for the average European consumer[18].

4 PLANT SECONDARY METABOLITES

Plant secondary metabolites are naturally occurring substances produced by plants to protect themselves against predators, diseases, or environmental stressors. These compounds can contaminate food and feed products, posing potential risks to consumers of various ages and dietary patterns[1].

4.1 Pyrrolizidine Alkaloids

Ragwort (*Senccion serradalis*) is one of the many plants that produces these protective compounds called pyrrolizidine alkaloids. These substances deter predators, such as caterpillars and humans, by rendering plants unpalatable or edible. While only 30 among these 600 pyrrolizidine alkaloids pose a significant threat to food and feed safety, high levels of contamination can cause acute liver poisoning in humans, potentially leading to death. However, for European consumers, this potential risk is currently low[25]. The International Agency for Research on Cancer (IARC) classifies some pyrrolizidine alkaloids as "possibly carcinogenic to humans" (Group 2B).

4.2 Tropane Alkaloids

More than 200 distinct tropane alkaloids exist within the vast array of plants, including those in grain fields like Datura. During harvesting processes, these unwanted plants' seeds and consequently their alkaloid-containing compounds end up in cereal products. A few tropane alkaloids have received considerable scientific attention, despite being produced by some food crops such as potatoes. Acute exposure to these alkaloids can result in neurological consequences for humans. Currently, due to poor occurrence data, only the dietary exposure for toddlers has been assessed indicating a potential risk[26]. However, based on the recent European-wide survey many tropane alkaloids are present in a range of foods, some with high levels[27]. This suggests that also other consumers may be at a potential risk.

4.3 Erucic Acid

Erucic acid is a natural component found in high levels within vegetable oils and fats, derived from cruciferous plants like canola (rapese) and mustard. Chemically, this compound forms a long-chain, monounsaturated omega-9 fatty acid. Excessive exposure to erucic acid can negatively impact human health by contributing to fatty heart disease. However, for the average European consumer of all ages, this poses not a potential risk for average European consumers[28-29].

4.4 Cyanogenic Glycosides

Cyanogenic glycosides constitute a diverse group of natural toxins, each containing one alcohol (sugar) molecule and a carbohydrate (carbohydrate) molecule, along with a cyanide group. In this state, the compound remains non-toxic. During enzymatic degradation processes, it releases toxic hydrogen cyanide (HCN), also known as prussic acid. The conversion to hydrocyanic acid occurs first through an enzyme that cleaves the corresponding sugar—often glucose.

A significant mention goes to amygdalin, found within bitter almonds and apricot kernels. When raw apricot kernels are chewed and ground, hydrocyanic acid is released from cyanogenic glycosides. In young children, even one small kernel can result in negative health effects, while adults can safely consume either three small kernels or less than half of a large kernel. Human exposure to hydrocyanic acid can result in high acute toxicity and even death. However, limited data are available for the chronic toxicity of cyanide to determine whether there is a potential risk for European consumers[20].

5 MARINE BIOTOXINS

Marine biotoxins pose an invisible yet significant risk to both marine life and human health. With approximately 5,000 algae species inhabiting the world's oceans and seas, around 300 of them can reach high concentrations leading to discoloration of large water bodies, such as red tides[1]. A subset of these algae produce toxic secondary metabolites – marine biotoxins – when in full bloom. These toxins accumulate in the tissues of shellfish and other filter feeders, which consume these algae, but also in fish and other seafood.

Marine biotoxins are highly potent substances that can cause acute symptoms upon ingestion by humans, ranging from mild tingling or numbness around the lips to death. To ensure public safety, shellfish-growing areas and shellfish are regularly tested for marine biotoxin contamination before being distributed to consumers. However, the levels of these toxins can vary widely depending on seasonal and annual climatic conditions, potentially leading to inconsistent dietary exposure and associated health risks.

In European waters, saxitoxin, okadaic acid, and domoic acid are the most prevalent marine biotoxins. While chronic health risks for average seafood consumers remain unknown due to insufficient data, those who consume large quantities of shellfish may face potential harm as EU maximum levels do not always provide sufficient protection. Additionally, some marine biotoxins lack legal limits in the EU, but their prevalence could change with climate shift.

Cooking methods like thermal processing can impact toxin levels in shellfish, either increasing or decreasing them[30]. Furthermore, cyanobacteria – also known as blue-green algae – found in surface waters and the marine environment can produce cyanotoxins that may contaminate drinking water and food. However, the exposure levels for Europeans remain uncertain[31]. The growing popularity of aquaculture products from Asia could potentially lead to significant exposure due to increasing consumption.

6 RISK RANKING AND CONCLUSIONS

In our research, we endeavored to arrange the potential chronic risks of identified contaminants based on both the type of harmful effects they elicited and their daily intake via food consumption. It is important to note that our ranking only includes contaminants recognized as posing chronic risks to adults by the European Food Safety Authority (EFSA), with those presenting low risks excluded[1]. This ranking of chronic chemical food safety risk for average European consumers did not consider uncertainties in EFSA's risk assessments, such as missing toxicity or occurrence data. As such, this risk ranking should be viewed as indicative.

First, contaminants derived from food processing hold the highest potential chronic risks. This is due to their genotoxic and carcinogenic properties, though these effects have not been definitively proven in humans. Their widespread presence in various daily consumed foods further underscores their significance. Second place is occupied by aromatic petroleum hydrocarbons, owing to their genotoxicity and carcinogenicity, although human evidence of these effects is lacking[1]. These contaminants are ubiquitous in numerous foods.

“Only” ranked third on our list are aflatoxins, which pose a high risk due to their significant carcinogenic potency causing liver cancer in humans. Europeans consume cereal-based foods in large quantities, making them the primary source of exposure to these contaminants. However, nuts and corn, more commonly contaminated with aflatoxins, are less frequently consumed in Europe.

Contaminants including dioxins, dioxin-like polychlorinated biphenyls, nickel, and a brominated flame retardant rank fourth based on their prevalence in many daily consumed foods. Despite the genotoxic and carcinogenic effects of this group of plant toxins, pyrrolizidine alkaloids occupy the fifth position due to their limited sources – tea, honey, or herbs – of human exposure[1,20].

It should be emphasized that the implications of chronic exposure to mixtures of toxic substances in our daily food intake remain unclear. Notably, several contaminants mentioned above possess genotoxic and carcinogenic properties, potentially increasing the risk from combined exposure to these substances beyond current individual chemical assessments[20].

7 CONCLUSIONS FOR EUROPEAN CONSUMERS

In conclusion, European consumers benefit from stringent food safety regulations at both national and European levels, ensuring that the food supply is safer than ever before. However, despite these efforts, it's essential to acknowledge that complete freedom from toxins in our food is an unattainable goal. Modern analytical techniques enable the detection, identification and quantification of contaminants in increasingly smaller concentrations, making it crucial for regulatory bodies to continuously update their standards and guidelines.

An emerging area of concern is the health risks associated with exposure to mixtures of chemical contaminants – so-called 'toxic cocktails.' These combinations can interact in complex ways that may lead to additive or even synergistic effects, posing a potentially greater risk than the risks assessed for individual chemicals. For instance, some contaminants can act as endocrine disruptors, altering hormonal balance and increasing susceptibility to other toxicants.

The potential health risks from food contamination are further compounded by climate change. Rising temperatures, altered precipitation patterns, and increased frequency of extreme weather events can impact agricultural practices and lead to accumulation of toxic compounds in food. It has also been reported that pathogenic microorganisms and plant pest are moving towards the poles at a velocity of 3~5 km per year[32] which will increasingly lead to unprecedented high levels of aflatoxins even in middle Europe.

It is, however, anticipated that future EU risk-management measures will lead to reduced dietary exposure of European consumers to chemical contaminants[33]. For instance, the European Food Safety Authority (EFSA) regularly updates its guidance values for contaminants based on new scientific data and evolving knowledge of their health risks. Moreover, regulatory bodies are continuously working to improve farming practices, reduce reliance on harmful pesticides, and promote cleaner production methods to minimize contaminant accumulation in food.

In conclusion, while European consumers can take comfort in the comprehensive food safety regulations in place, it's essential to remain vigilant about potential health risks from chemical contaminants in our food. By focusing on a balanced diet rich in whole foods and limiting ultra-processed items, consumers can minimize their exposure to these contaminants while supporting overall health and wellbeing. Additionally, the ongoing efforts of regulatory bodies to improve food safety standards and reduce contaminant accumulation are to contribute to a healthier and safer food supply for generations to come.

REFERENCES

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