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Food Additives and Contaminants: Part B Surveillance

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https://doi.org/10.1080/19393210.2023.2227961

FOOD ADDITIVES & CONTAMINANTS: PART B
2023, VOL. 16, NO. 3, 301–309
https://doi.org/10.1080/19393210.2023.2227961

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Occurrence and associated health risks of pyrrolizidine alkaloids in supplements marketed in Ghana for improved sexual performance

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ABSTRACT

Pyrrolizidine alkaloids (PAs) are noted for their hepatotoxic, genotoxic, and carcinogenic effects in animals and humans following metabolic activation in the liver. In this study, herbal supplements sold in Ghana for sexual improvement were analysed for the presence of 64 PAs using LC-MS/MS analysis. Up to 17 different PAs were identified in 19 out of the 37 samples analysed. The sum of PAs in samples ranged from 5 to 3204 µg kg^{-1}. Since the PA content in the herbal medicinal preparations was generally lower than in honey samples, their presence was mainly attributed to cross-contamination. The observed levels would result in estimated daily intakes from 0.01 to 12 µg per day or 0.0002 to 0.2 µg kg^{-1} bw day^{-1} for a person weighing 70 kg. The margins of exposure ranged from 1200 to 1,400,000 with eight samples showing values below 10,000, thus indicating a health concern.

ARTICLE HISTORY
Received 19 February 2023
Accepted 18 June 2023

KEYWORDS
Herbal supplements; pyrrolizidine alkaloids; health risk; aphrodisiacs; Ghana

Introduction

Pyrrolizidine alkaloids (PAs) are heterocyclic organic secondary metabolites produced by plants for defensive roles (Ober and Kaltenegger 2009). They are found in various plant families including Apocynaceae, Asteraceae (Compositae), Boraginaceae, Leguminosae (Fabaceae), and Orchidaceae (Langel et al. 2011). These toxins occur in botanical preparations when PA-containing plants are used, or when products are contaminated with PA-producing plants during harvesting or processing. PAs may occur as tertiary amines (free base) or as their *N*-oxide (i.e. PA-*N*-oxide or PANO) (Hartmann and Witte 1995; Langel et al. 2011; Kaltner et al. 2019). More than 660 different PAs have been associated with over 6000 plant species, which corresponds to more than 3% of the flowering plants (Smith and Culvenor 1981). Their structures and classifications have been extensively discussed and reviewed (Stegelmeier et al. 1999; Moreira et al. 2018; Dusemund et al. 2018; Chen et al. 2019).

The Scientific Panel on Contaminants in the Food Chain (CONTAM Panel) of the European Food Safety Authority performed a risk assessment and concluded that exposure to PAs could present both acute and chronic effects in consumers (EFSA 2011; EFSA et al. 2017). Acute human exposure to toxic PAs is characterised by hepatic sinusoidal obstruction syndrome (HSOS), which may induce severe liver injury and lead to liver cirrhosis and failure (hepatic veno-occlusive disease or HVOD). Chronic exposure may lead to abnormalities in the liver and lungs, including tumours and the development of pulmonary arterial hypertension. In particular, the 1,2-unsaturated PAs (e.g. riddelliine, lasiocarpine, and monocrotaline) are considered to be genotoxic carcinogens. Metabolic activation in the liver by cytochrome P450 monooxygenases results in the formation of highly reactive electrophilic pyrrolic intermediates (Fu et al. 2004; Dusemund et al. 2018). These metabolites (alkylating agents) can bind to endogenous nucleophiles such as proteins and nucleic acids, resulting in cell damage, cell death, and/or induction of tumour formation (Mattocks 1986; Winter and Segall 1989; Fu et al. 2002; Gottschalk et al. 2018). PA-*N*-oxides can be reduced to their corresponding tertiary amines in the gut and liver (Gottschalk et al. 2018). Toxicity of individual PAs depends on the dosage, nature and duration of exposure, individual susceptibility, rate of bioactivation to pyrroles, and chemical reactivity of the pyrrole produced (Mattocks 1986; Roeder 1995; Stegelmeier et al. 1999).

Herbal medicinal preparations have a long tradition of use, particularly in West Africa, and are still used extensively as an alternative to more expensive or less available modern medication (Komlaga et al. 2015;

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Supplemental data for this article can be accessed online at https://doi.org/10.1080/19393210.2023.2227961.

Letsyo et al. 2017a). Several studies have reported the presence of PAs in herbal infusions, medicines, and dietary supplements from many countries including Ghana (Letsyo et al. 2017a, 2017b; Mulder et al. 2018; Picron et al. 2018; Chen et al. 2019; Kaltner et al. 2020; Suparmi et al. 2020). Letsyo et al. (2017a, 2017b) focused on a number of widely used and licenced herbal medicinal products obtained from drugstores in Ghana, in addition to honey. According to the study, approximately 60% of the herbal preparations contained PAs. Since the PA content in the herbal medicinal preparations was generally lower than in honey samples, their presence was mainly attributed to cross-contamination. Nonetheless, there is the likelihood that these compounds' presence may result from raw material contaminated with PAs at varying levels. However, for most of the selected products, the labels did not indicate the presence of PA-producing plants (Letsyo et al. 2017a). It should be noted that in this study the LC-MS/MS method used determined the sum of PAs, meaning that identification of the PA-containing plants was not our main objective.

Despite these studies, there is a lack of data on the presence of PAs in herbal products/supplements sold for sexual enhancement currently available on the Ghanaian market. The present study is part of a wider approach to investigating the presence of adulterants and contaminants in plant supplements sold on the Ghanaian market for improving sexual performance (Akuamoa et al. 2021, 2022a, 2022b). The objective of the current study was to analyse the selected samples for the potential presence of PAs. Based on the results, a risk assessment was performed using recommended daily intakes of the respective botanical preparations to estimate exposure levels of consumers and resulting health risks based on the estimated margins of exposure (MOE).

Materials and methods

Supplements

Of the 40 herbal supplements previously examined by Akuamoa et al. (2021), 37 were investigated in this study. Supplementary Table S1 shows the list of supplements and their corresponding IDs, country of origin, composition, intended use, directions for use and other relevant information. These samples were purchased from various markets, drugs, and chemical shops in Accra, although some were produced in other countries. The criteria for sample selection were mainly based on their intended use, i.e. for improving sexual performance. These samples were sold without any form of regulations and were purchased without any form of prescription. This meant consumers could easily have access to these products without any restriction. The contents of each capsule were poured into zip-lock bags and mixed, while liquid-based supplements were manually agitated for 5 minutes prior to preparation.

Chemicals and reagents

A total of 64 PA standards were used in the analysis. Details on vendors, purity, and CAS numbers can be found in supplementary Table S2. The purity of the standards was at least 95%. Spartioidine *N*-oxide was synthesised in-house following the method of Chou et al. (2003). PA stock solutions of 200 μg mL^{-1} were prepared in methanol. A mixed PA solution of 1 μg mL^{-1} in methanol prepared from each stock solution was used to spike the supplements. Methanol and acetonitrile, both of LC-MS grade, were obtained from Actu-All (Oss, The Netherlands). Formic acid and ammonium carbonate were of analytical grade and purchased from Sigma-Aldrich (Zwijndrecht, The Netherlands). Deionised water from a Milli-Q Ultra Pure system (Millipore, Bedford, MA, USA) with a minimum resistance of 18.2 M was used as a solvent.

Compound extraction and purification

Compound extraction was performed based on an in-house validated method described by Chen et al. (2019). Briefly, 1 g of solid or 1 mL of liquid sample was either weighed or aliquoted in duplicate into extraction tubes. One of the test samples was spiked with 250 μg PAs kg^{-1} by adding 250 μL mixed PA standard solution. To each tube, 20 mL of a 0.2% formic acid solution in water was added and the samples were agitated in a rotary tumbler for 30 min and subsequently centrifuged for 15 min at 3500 *g*. Next, 5 mL of each sample extract was aliquoted into new tubes, where the extracts were neutralised to a pH of 6–8 with 350 μL of 1 M ammonium carbonate solution and subsequently centrifuged at 3500 g for another 15 min.

Each extract was purified using solid-phase extraction (SPE) with Strata-X Polymeric reversed-phase cartridges, 200 mg per 6 mL of Phenomenex (Palo Alto, CA, USA). The cartridges were pre-conditioned with 6 mL methanol, followed by 6 mL water. The whole content of each neutralised extract was passed through individual cartridges and subsequently washed with 6 mL 1% formic acid, followed by 6 mL water. Cartridges were dried for 10 min under reduced pressure using an SPE vacuum manifold. Next, the compounds of interest

were eluted with 6 mL of methanol. Eluates were subsequently dried under a continuous stream of nitrogen at 50°C using a TurboVap (Biotage, Uppsala, Sweden). Resultant residues were filtered through 0.45 µm PTFE filter vials (UniPrep, Whatman, Maidstone, UK) after reconstitution with 500 µL methanol/water 10/90, v/v. Vials were closed using a compressor and stored at −20°C until analysis.

LC-MS/MS analysis

The LC-MS/MS system consisted of a Waters Acquity UPLC coupled to a Xevo TQ-S tandem mass spectrometer, equipped with a UPLC BEH C18 analytical column (150 × 2.1 mm with 1.7 µm particle size) from Waters (Milford, MA, USA). Column and sample temperature were set at 50°C and 10°C, respectively. The analytes were eluted with a gradient programme consisting of two mobile phases: water containing 10 mM ammonium carbonate pH 9 (A) and acetonitrile (B) and a flow rate of 0.4 mL min^{-1}. The linear gradient started at 0% B, increased to 5% B at 0.1 min, 10% B at 3.0 min, 24% B at 7.0 min and 70% B at 12.0 min. Finally, B was decreased to 0% at 12.1 min and kept at this composition for 2.1 min. The injection volume was 2 µL of a sample extract.

The linearity of the LC-MS/MS was assessed using matrix-matched standards (MMS) with eight data points, to confirm the accuracy of the sample pretreatment. To achieve this, eight test samples (1 g) of a previously tested supplement with no indication of PAs (<LOD) were spiked with a mixture of the PA standards in a concentration range of 0 to 1000 µg kg^{-1}. The MMS samples were treated and analysed following the procedure described above. The LOQ was 5 µg kg^{-1} for individual PAs in solid samples and 5 µg L^{-1} in liquids.

PAs in samples were detected and confirmed by comparing their retention times and ion ratios with those of the calibration curves of compounds in the MMS, using two MRM transitions measured per analyte. In supplementary Table S3, the mass spectrometric settings for each analyte are given. Individual sample concentrations were determined based on each sample's single-level standard addition (250 µg kg^{-1}).

Samples S2, S6, S12, S26, S27, and S38 contained one or more PAs that exceeded the standard addition level of 250 µg kg^{-1}. These samples were reanalysed by means of a standard addition to the final extract. Three aliquots (50 µL) were taken from these extracts and transferred to new vials. The aliquots were spiked with, respectively, 6.25, 25, and 62.5 µL mixed PA solution. A fourth aliquot of 50 µL was left unspiked. Water was added to obtain a final volume of 250 µL. Data were processed using the TargetLynx 4.2 software (Waters Corporation, Milford, MA, USA).

Calculation of estimated daily intake

The estimated daily intake (EDI), expressed as µg per day, was calculated by *EDI = Total PAs xAverage weight xNo. of doses*, where total PAs is the total concentration of the PAs in each sample by LC-MS/MS, expressed as µg kg^{-1} (solid samples) or µg L^{-1} (liquid samples); average weight is the average weight per dose unit expressed in kg or L; No. of doses is the recommended number of doses per day. For the daily exposure expressed as µg kg^{-1} bw per day the EDI was divided by a body weight of 70 kg (*assumed weight of a consumer*).

Safety assessment

Regarding the genotoxic carcinogenic properties, the margin of exposure (MOE) approach was used for risk assessment of the 1,2-unsaturated PAs in samples, as recommended by the European Food Safety Authority (EFSA 2005). To assess the potential risk of PAs as a result of chronic exposure, EFSA et al. (2017) established a benchmark dose ($BMDL_{10}$) of 237 µg kg^{-1} bw per day, which is the lower bound of the dose that showed a 10% increase in the incidence of liver tumours in rats treated with riddelliine (NTP 2003), as the reference point for calculating the margin of exposure (MOE). The MOE is calculated by dividing this $BMDL_{10}$ by the calculated exposure. For genotoxic carcinogens, EFSA (2005) considers a MOE larger than 10,000 generally of a low health concern.

Results and discussion

Pyrrolizidine alkaloid levels in supplements

The 37 supplements were analysed for the presence of sixty-four 1,2-unsaturated PAs (Supplementary Table S2). This is the largest set of PAs available in our laboratory for quantitative analysis of herbal samples. The set covers the three main groups of 1,2-unsaturated PAs, monoesters (14 standards), open-chained diesters (12), and cyclic diesters (38). For all PA standards, the tertiary amine and corresponding *N*-oxide forms were available, except for senkirkine and otosenine, which occur only in their free base form. All but two isomeric PAs were at least partially chromatographically separated in a single run. The monoesters lycopsamine and indicine could not be separated, but the corresponding *N*-oxides were well separated. Therefore, in those samples where a peak

was detected at the retention time for the lycopsamine/indicine pair, the identity of the isomer was deduced from the presence of the corresponding *N*-oxide. Lycopsamine *N*-Oxide and indicine *N*-Oxide did not co-occur in any of the selected samples. Overall, 19 (51%) out of the 37 supplements contained 17 different PAs (10 free bases and 7 *N*-oxides) with concentrations above the LOQ, i.e. 5 μg kg^{-1} (Table 1).

The sum of PAs in their free bases ranged from 7 to 2513 μg kg^{-1}, whereas the *N*-oxides ranged from 13 to 1269 μg kg^{-1}. Overall, the total PA concentration (i.e. the sum of free bases plus *N*-oxides) ranged from 7 to 3204 μg kg^{-1}. Sample S12 contained the highest level (2513 μg kg^{-1}) of free bases followed by S38 (1540 μg kg^{-1}). With respect to PA *N*-oxides, samples S27 (1269 μg kg^{-1}) and S26 (825 μg kg^{-1}) contained the highest levels. Total PA content was highest in S12 (3204 μg kg^{-1}) followed by S27 (1859 μg kg^{-1}). The average PA level (300 μg kg^{-1}) was substantially higher than that reported by Letsyo et al. (2017) in 70 Ghanaian herbal medicinal products, which was 26 μg kg^{-1}. Overall, in eight samples of the current survey, the PA content was above the maximum level (ML) of 400 μg kg^{-1} for herbal supplements, recently established by the European Commission (EC 2020). For comparison, in the study of Letsyo et al. (2017a), only one sample (1290 μg kg^{-1}) would have exceeded this ML.

Pyrrolizidine alkaloid profiles

Interestingly, all identified PAs in the 19 positive samples were open-chained monoesters and diesters of both retronecine- and heliotridine-type necine bases. Cyclic diesters were not found in any of the supplements, except for traces of monocrotaline in sample S27. In Figure 1, samples with similar PA profiles have been grouped based on their relative contributions to the total PA. Nine of the 19 positive samples contained a combination of rinderine and intermedine and their *N*-oxides (Figure 1a). Smaller amounts of lycopsamine and its N-oxide were also present. In sample S16, indicine and its *N*-oxide were present, possibly due to a co-contamination with *Heliotropium indicum*. In all these samples, the PA tertiary amines and *N*-oxides were present in approximately equal amounts. The combination of rinderine and intermedine as primary compounds is not commonly found in Boraginaceae species (El-Shazly and Wink 2014); however, they do co-occur in species of the Eupatorieae tribe, such as in *Chromolaena odorata (Eupatorium odoratum)*, as reported by Biller et al. (1994) and Roeder and Wiedenfeld (2009). *Chromolaena odorata* is a species that is common in Ghana and used as an ingredient in herbal preparations to treat various ailments, including malaria (Komlaga et al. 2015; Letsyo et al. 2017a). *Chromolaena odorata* is considered a highly invasive weed in Ghana and other parts of West Africa (Timbilla and Lawson 2014). It was identified as the predominant source of pollen in honey by PA-producing plants in a study by Letsyo et al. (2017b).

Two samples (S23, S38) had a combination of europine, heliotrine and lasiocarpine, with traces of rinderine and heliotrine *N*-oxide (Figure 1b). Two other samples (S26, S28) contained primarily indicine and its *N*-oxide, with traces of rinderine, intermedine, and its *N*-oxide (Figure 1c). Europine, heliotrine, lasiocarpine, and indicine are typically found in *Heliotropium* species (El-Shazly and Wink 2014; Shimshoni et al. 2021). Indicine has only been reported for a few species, including *H. indicum*, a species that is native to Ghana (Singh et al. 2005; Timbilla and Lawson 2014; Letsyo et al. 2017b). Like *C. odorata, H. indicum* is also used as an ingredient in herbal preparations (Komlaga et al. 2015; Fayed 2021). However, the two different profiles seem to indicate that different *Heliotropium* species are present in the samples. According to the African Plant Database, other *Heliotropium* species that occur in West Africa are *H. bacciferum, H. ovalifolium, H. ramosissimum, and H. supinum*. Except for *H. ovalifolium*, the other species are known to produce heliotrine, europine, and lasiocarpine (El-Shazly and Wink 2014).

Finally, one sample (S12) contained predominantly echinatine and its *N*-oxide together with traces of rinderine, intermedine, lycopsamine, and their *N*-oxides (Figure 1d). Another common species in Ghana, *Ageratum conyzoides*, does contain echinatine and lycopsamine as primary PAs (Timbilla and Lawson 2014; Suparmi et al. 2020). This species is also a known ingredient of herbal preparations (Komlaga et al. 2015; Letsyo et al. 2017a), and its pollen was also present in some of the honey samples produced in Ghana (Letsyo et al. 2017b).

One crucial question is whether the source of PAs in the supplements could be related to one or more of the plant ingredients mentioned on their labels. A total of 72 different ingredients were indicated on the labels of the 37 samples. Only one ingredient, *H. indicum*, is a known PA-producing plant. Roeder and Wiedenfeld (2009) addressed the hepatoxic effects of alkaloids in *H. indicum* and discouraged their oral intake. Although this plant was mentioned on the label of S39, this supplement only contained trace amounts of rinderine. Six samples (S1, S12, S17, S20, S23, S39) contained plants belonging to the Fabaceae plant family (*Pueraria tuberosa, Abrus precatorius, Dalbergia saxatilis*, *Astragalus root, Mucuna pruriens*). However, none of these

Table 1. Identified PAs (free bases and *N*-oxides) and their respective total concentrations (μg kg^{-1}) in positive samples.

List of samples	7-Acetylintermedine	7-Acetylintermedine N-oxide	Echinatine	Echinatine N-oxide	Europine	Heliotrine	Heliotrine N-oxide	Indicine	Indicine N-oxide	Intermedine	Intermedine N-oxide	Lasiocarpine	Lycopsamine	Lycopsamine N-oxide	Monocrotaline	Rinderine	Rinderine N-oxide	Sum Free Bases	Sum *N*-oxides	Sum 64 PAs
S2										192	240		6	9		159	393	357	643	1000
S5										42	56					51	91	93	147	240
S6										202	202		9	7		165	403	376	612	988
S8										111	42		5			146	138	262	179	442
S9			11															11		11
S12			2364	609						14	36		17	11		117	34	2513	691	3204
S16								5	14	12	17					22	50	39	82	121
S17													7					7		7
S18																7		7		7
S21										83	125		21	11		67	161	171	297	468
S23					10	44												54		54
S26			5					115	802	11	23							130	825	956
S27	6	12		6						265	389		48	53	8	263	809	590	1268	1859
S28								24	85							6		30	85	114
S29																5		5		5
S30										23	19		5			14	21	42	40	82
S37										10	11					10	17	19	29	48
S38			8		182	1199	13					133				18		1540	13	1553
S39																9		9		9

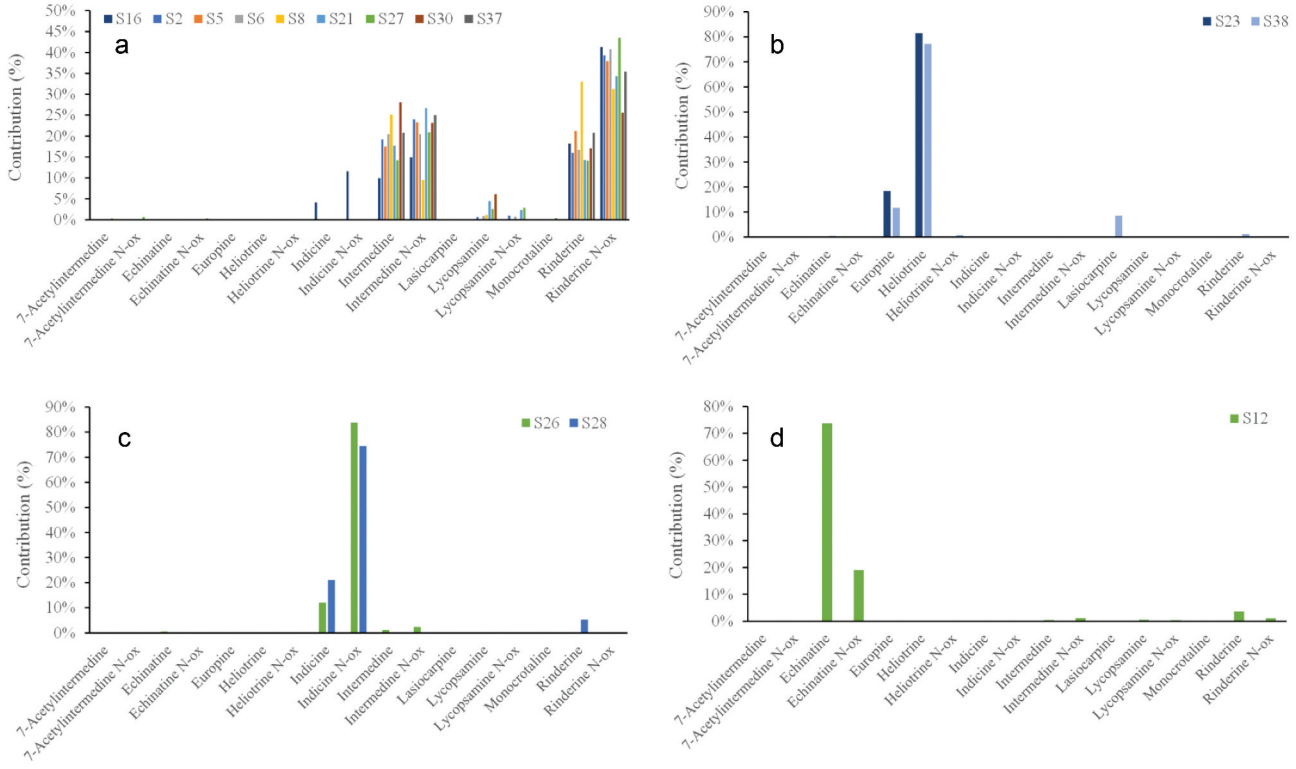

Figure 1. PA profiles found in samples based on contribution to the sum of PAs and grouped according to similarity, with (a) nine samples with primarily intermedine, rinderine, and their *N*-oxides, (b) two samples with europine and heliotrine, (c) two samples with indicine and its *N*-oxide, (d) one sample with echinatine and its *N*-oxide.

plants is known to contain PAs. Three other samples (S6, S21, S38) produced from the same plant materials (*Penianthus zenkeri, Clausena anisata*), contained different amounts of PAs. In two of these samples (S6, S21) four similar PAs (intermedine, rinderine, and their *N*-oxides) were identified, while the PAs identified in S38 were different. Combined with the relatively low PA levels, these observations point to contamination with PA-containing plants during production.

Risk assessment

The estimated daily intake (EDI) of PAs (μg day^{-1}) was calculated based on the recommended daily dose and using an average body weight of 70 kg, by *TotalPAsxAverageweightxNo.ofdoses* (Table 2). The EDIs ranged from 0.01 to 12.42 μg day^{-1}. When taking the bodyweight into concern, these values were ranging from 0.0002 to 0.19 μg kg^{-1} bw day^{-1}, with S27 resulting in the highest exposure. Generally, samples with higher concentrations showed higher exposure; however, some samples with relatively low PA concentrations also resulted in relatively high intakes due to high recommended intakes (e.g. S30). Even the highest calculated intake of 0.19 μg kg^{-1} bw per day was well below the 15 μg kg^{-1} bw day^{-1}, which is the exposure likely to cause hepatic veno-occlusive disease (HVOD) in humans (WHO-IPCS 1988; EFSA 2011; EFSA 2020).

The International Agency for Research on Cancer (IARC 1976) classified certain PAs such as lasiocarpine and monocrotaline as possibly carcinogenic to humans (Group 2B). Furthermore, due to the genotoxic and carcinogenic effects of 1,2 unsaturated PAs in general, EFSA (2011; EFSA et al. 2017) concluded that these compounds are genotoxic carcinogens and as a result, no safe threshold value can be derived. Therefore, the margin of exposure (MOE) approach is best suited when characterising the risk upon exposure to products containing PAs. MOE values were determined by dividing the $BMDL_{10}$ of 237 μg kg^{-1} bw day^{-1}, derived by ESFA et al. (2017) for liver tumours in rats exposed to riddelliine, by the estimated intakes (Table 2). The calculated MOE values ranged from 1,200 to 1,400,000, where eight samples had MOE values below 10,000, which according to EFSA (2005) implies a health concern. It should be noted that this approach assumes life-long exposure, which in the case of these types of supplements is likely to present a worst-case scenario. On the other hand, in toxicological studies with lasiocarpine and riddelliine (NTP 1978, 2003), many

Table 2. Levels of PAs in positive samples, dose weight, and number of doses per day, resulting EDIs and exposure per kg bw per day of a 70 kg consumer and the MOEs.

Sample	ΣPAs (μg kg^{-1})	Dose (g)	No. of doses per day	EDI (μg/day)	Exposure (μg/kg bw/day)	MOE
S2	1000	0.81	4	3.24	0.05	4,800
S5	240	1.01	4	0.97	0.01	16,000
S6	988	0.47	2	0.93	0.01	17,000
S8	442	2.01	6	5.33	0.08	2,900
S9	11	0.51	2	0.01	0.0002	1,420,000
S12	3204	0.74	2	4.74	0.07	3,300
S16	121	0.65	2	0.16	0.002	98,000
S17	7	1.10	4	0.03	0.0005	500,000
S18	7	0.65	4	0.02	0.0003	894,000
S21	469	0.97	4	1.82	0.03	8,500
S23	54	20	1	1.08	0.02	14,000
S26	956	1.10	2	2.10	0.03	7,300
S27	1859	1.67	4	12.42	0.19	1,200
S28	114	2.13	6	1.46	0.02	10,600
S29	5	1.09	4	0.02	0.0003	740,000
S30	82	30	4	9.79	0.15	1,600
S37	48	2.03	4	0.39	0.01	39,700
S38	1553	1.47	4	9.13	0.14	1,690
S39	9	1.70	4	0.06	0.001	240,500

animals died before the end of the study due to liver tumours. This implies that also shorter exposure may result in these tumours. There is no generally accepted method to correct for a shorter exposure duration.

Another important issue is that in the above-mentioned calculations, the various PAs detected in the samples were assumed to have equal toxic potencies. In practice, there are strong indications that most PAs are less toxic than riddelliine for which the reference point ($BMDL_{10}$) was derived. Merz and Schrenk (2016) evaluated the available information and proposed relative potency factors (RPFs) for a number of PAs. Similar RPFs were also established by Louisse et al. (2019) based on genotoxic potencies of PAs in the human liver HepaRG cells. The latter study also proposed interim RPFs for some additional PAs, like rinderine. PA *N*-oxides assumed the same potency as their free bases. The RPFs for the different PAs detected in the supplements, varying between 0.01 and 1, were applied on the level of each PA as shown in supplementary table S4. The resulting equivalent levels for the sum of PAs varied between 0.1 and 938 μg kg^{-1}, the highest level still for S12. For this sample and also other ones revealed in Figure 1a, rinderine and its N-oxide became the most relevant PA, due to the lower potency of intermedine and its N-oxide. Using these levels expressed in riddelliine equivalents, EDIs decreased by a factor of 2.8 to 100, while the MOE values increased by the same factors. Nevertheless, the MOE values for S27 and S38 were still below 10,000, indicating a health concern upon life-long exposure (supplementary table S4). At the moment, there is no international consensus about the use and magnitude of the proposed RPFs in risk assessment or risk management of toxic PAs in botanical preparations. Like Letsyo et al. (2017a), the current study points to the possible contamination of supplements with toxic PAs. In this study, the question remains if herbal preparations are intentionally prepared using PA-containing herbs since studies have shown that PA levels in such products can be considerably higher (Fu et al. 2002; Mulder et al. 2018; Suparmi et al. 2020).

Conclusions

This study is part of a project assessing the safety of plant supplements sold in Ghana to improve sexual performance (Akuamoa et al. 2021, 2022a, 2022b). The current objective was to analyse the selected supplements for the potential presence of PAs to assess the possible risk for users upon exposure. The study revealed the presence of PAs in almost 50% of the supplements, which in almost all cases did not correlate to the ingredients listed on their labels. The relatively low levels determined implied that the source is likely related to the contamination of ingredients with PA-containing plants. While the estimated intake levels were generally low, exposure levels for eight samples pointed to a potential health concern.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Funding

This work was supported financially by the Dutch organisation for internationalisation in education (Nuffic) as project number 61.390.30.270.

Collaboration

This project is a collaboration between Wageningen Food Safety Research and the Department of Toxicology at Wageningen University and Research.

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