Journal of Elementology ISSN 1644-2296

Chmielewski J., Nowińska L., Gworek B., Goś P., Gonczaryk A., Florek-Łuszczki M. 2021.
Primary Aromatic Amines (PAAs) as a Threat to the Health of Consumers.
J. Elem., 26(2): 463-473. DOI: 10.5601/jelem.2021.26.2.2148

RECEIVED: 6 April 2021
ACCEPTED: 30 May 2021

REVIEW PAPER

PRIMARY AROMATIC AMINES (PAAS) AS A THREAT TO THE HEALTH OF CONSUMERS*

Jarosław Chmielewski[1], Lidia Nowińska[2], Barbara Gworek[3], Piotr Goś[4], Agnieszka Gonczaryk[5], Magdalena Florek-Łuszczki[6]

[1,2] College of Rehabilitation in Warsaw, Poland
[3] Institute of Environmental Protection-National Research Institute, Warsaw, Poland
[4] Warsaw School of Management – Higher School of Management, Warsaw, Poland
[5] Marshal's Office in Warsaw, Poland
[6] Department of Medical Anthropology, Institute of Rural Health, Lublin, Poland

Abstract

The article presents the current knowledge regarding the health risks related to the exposure to primary aromatic amines (PAAs), which are found in products designated to come in contact with food. Food safety, including products designated to come in contact with it, is one of the elements of health care policy adopted by the member states of the European Union (EU) in the broad context of public health. Materials either used for packaging or as their own entity, appliances, tableware, kitchenware or other products intended to come in contact with food must meet the requirements outlined in the legal regulations operating in the EU, and in the law of its member states. Diversity of raw materials in products coming in contact with food makes them a causal factor in the contamination of food with substances that are harmful to health. In an attempt to protect food and guaranteeing its safety, the Rapid Alert System for Food and Feed (RASFF) has been established in the EU. This system is used for the exchange of information concerning the hazards detected in food, animal feed, and materials designated for coming in contact with food products. Like food, products that come in contact with it are under official control and the RASFF system. The large-scale use of chemical compounds in the production of articles which come in contact with food entails their significant effect on the safety and health quality of food products. Food contaminated in this manner may have adverse effects on the health of consumers. Health complications may manifest as cancers, congenital disorders, fertility issues as well as damage to the nervous and immune systems. One

Jarosław Chmielewski, PhD, College of Rehabilitation in Warsaw, Kasprzaka 49 St., 01-234 Warsaw, Poland, e-mail: j.chmielewski@ios.gov.pl

* The project is financed from the Research Fund of the College of Rehabilitation in Warsaw, which is intended to support the continuity and development of the university's scientific research.

of the groups of chemical compounds identified in products coming in contact with food includes primary aromatic amines (PAAs).

Keywords: primary aromatic amines (PAAs), food contact materials, food, health, migration.

INTRODUCTION

The safety of food products is not just the subject of legal regulations but also the object of supervision from government institutions established for this purpose.

Actions with the purpose of ensuring the safety of food should take into consideration any and every kind of threat at every stage of production so that the final food product and the product designated to come in contact with it are entirely risk-free.

Other than supplying the organism with essential nutrients, food should be of adequate quality in terms of health and, first and foremost, ensure the safety of consumer health (Fung et al. 2018). It stems from the fact that food has become one of the main routes of people's exposure to foodborne diseases (Godfray et al. 2010, Fung et al. 2018).

Concerns over the safety of food and its potential adverse effects on health arise from a possibility of the contamination of food with chemical substances. This is related to the use of those substances in the stages of cultivation, production, distribution and selling of food. Thus, the aforementioned concerns become a relevant issue for public health.

In the past, the contamination of food and food products by chemical substances was the cause of many poisonings as well as related health problems among food consumers and their progeny (Eto 2000, Ikeda 2004, Li et al. 2013, El-Nezami 2013, Shimohata 2015).

It is estimated that 70% of food is packaged in packages made from plastic, mainly polymers, which have already become familiar (Nowotyńska et al. 2018). Polymers are regarded as non-toxic substances. Due to their structure, they are classified as macromolecular compounds which do not show the ability to migrate to food. However, it is micromolecular substances that may be a threat to consumer health due to their ability to migrate from packaging material to food (Latos et al. 2017).

The main aim of packaging designated to come in contact with food is the broadly understood protection of food products. However, instead of ensuring high quality of food products, their packaging is frequently a source of substances harmful to the health of consumers. The risk of migration of toxic substances from the packaging to food is the reason why the materials used in their production are subject to high standards related to ensuring the safety of food. The situation is similar in terms of products coming in contact with food.

Legal regulations applicable in the EU outline the general requirements that must be met by all final materials and products coming in contact with food, with or without print, regardless of the raw material type they were made from. Both materials and products coming in contact with food cannot pose a threat to the health of consumers (Regulation 2004, Commission Regulation 2011).

The EU's integrated food safety policy involves a wide range of activities in the context of public health. In order to ensure the establishment of effective control systems and assessment of compliance with EU norms regarding the safety and quality of food, the European Food Safety Authority (EFSA) has been established.

In the EU, the EFSA plays the role of the coordinator of activities taken to counteract arising threats in the area of food safety, and is responsible for the exchange of information between member states, which is necessary for the protection of consumer health (Costa et al. 2017).

The State Sanitary Inspection (SSI) is the counterpart of the EFSA in Poland in terms of public health activities, in the aspect of supervising health conditions of food and nutrition. The SSI's tasks include supervising the trade of products designated to come in contact with food.

The contamination of food by chemical substances is understood as every form of their migration to food as a result of the processes of production, modification, treatment, preparation, packaging, storage, transport and originating from environmental pollution (Ciecierska 2014).

The legislation on both the EU and national levels states that food contact materials (FCMs) made from plastics cannot release primary aromatic amines (PAAs), which are toxic compounds suspected to exhibit cancerogenic properties in humans (Regulation 2004, The Law 2006). Substances used in the production of FCMs from plastics are subject to authorization, which includes initial substances and additions (EFSA 2017).

SOURCES OF PAA RELEASE TO FOOD PRODUCTS

According to the literature, the source of PAA release to food products is polyurethane-based adhesives used in the production of multilayer foil used for packaging food, as well as azodyes, which can remain in the final pigments at trace levels and possibly migrate to food products from food packaging with print or tinted with this kind of dye (Lambertini et al. 2014).

PAAs are defined as chemicals having a primary amine (-NH_2) attached to an aromatic ring. They range from the simplest aniline to highly complex molecules with conjugated aromatic or heterocyclic structures and multiple substituents (Rubio et al. 2014).

PAAs include toluenodiamines (TDA) and methylenedianilines (MDA), such as 2,4-TDA, 2,6-TDA, 4,4'-MDA, 2,4'-MDA and 2,2'- MDA (Shahrestani et al. 2018).

PAA detection techniques, which are well known, allow for their identification in materials used for food contact.

Numerous studies show that PAA migration from products which come in contact with food (e.g., spatulas, whisks, spoons, kitchenware) to food products may happen as a result of their being left over after the process of their production or dyeing (Poças, Hogg 2007, Marchildon 2011, McCall et al. 2012, Lambertini et al. 2014, Paseiro-Cerrato et al. 2014, Rubio et al. 2014, Sanchis et al. 2019).

PAAs are substances contaminating food. Their migration to food may be traced back to coloured plastics, printed paper, kitchen utensils and elastic packaging. One of the sources of PAA release to food is polyurethane adhesives. Many cooking utensils are made of nylon, a material that may incorporate azodyes and PAAs as starting substances (Sendón et al. 2010, Trier et al. 2010, Pezo et al. 2012, Mattarozzi et al. 2013, Campanella et al. 2015, Shahrestani et al. 2018).

The relevant literature shows a possibility of a toxicological assay of significant PAAs in items made from plastics and products designated to come in contact with food, including packaging, paper, cardboard and napkins (Li et al. 2013, Xiao et al.2013, Yavuz et al. 2016, Merkel et al. 2018).

PAAs are a group of substances with adverse health effects, which are used in many commercial products, an some of these substances have cancerogenic properties (Perez et al. 2014).

According to RASFF data, 25% of the reports in the years 2010-2015 were related to PAAs, a common source of which were polyamide kitchen utensils (Sanllorente et al. 2016). In 2003-2021 (as of 23.03.2021), the RASFF system received 434 notifications from various EU countries regarding the migration of PAAs from materials designated to come in contact with food, wherein 25 were recorded in 2014, 18 in 2015, 17 in 2016, 13 in 2017 and 25 in 2018 (Perez et al. 2019, European Comission 2021,). Table 1 presents the products notified in the period between 17.01.2019 and 30.03.2021 in the warnings issued by the Chief Sanitary Inspectorate (GIS), which is the national representative of ESFA (GIS 2021).

EFFECT OF PAAs ON HEALTH

The negative effect on human health that chemical substances migrating to food from packaging and materials coming in contact with food is the subject of current research (Ochwanowska et al. 2019).

PAAs, e.g.: 4,4'-oxydianiline, 4,4'- methylenedianiline, 2,4-toluenodiamine, 3,3'- dimethylbenzidine, are substances suspected of exhibiting cancerogenic activity in the human body (Doe et al. 1995, Pawlicka et al. 2015). According to the EU regulations, compounds like these released from materials and plastic products to food or food simulants should not exceed the limit of quantification of 0.02 mg kg^{-1} (expressed as aniline) (Geueke, Muncke 2017).

Table 1

Migration of primary aromatic amines from food contact products

Product name	Date of issuing a warning	Producer/Country of origin
Tablespoon P02	04.03.2021	no data
Whisk P02		
Skimmer P02		
Ladle P02		
Spatula for Teflon P02		
Potato smashed P02		
Skimmer – black skimming spoon made of polyamide „Spatel Neberacka"	12.01.2021	Wenzhou Jinzhou Group Intl. Trade Corp. Ltd. Adr: Jinzhou Mansion, Wenzhou Road, Wenzhou China
Ladle	04.01.2021	no data
Skimmer	16.12.2020	no data
Fiskars Functional Form™ Spoon	17.11.2020	no data
Kitchen utensils – spatula	13.10.2020	no data
Teaspoon	04.09.2020	China
Odelo prestige quality line, sella, potato smasher	04.09.2020	China
Skimmer	29.06.2020	China
Skimmer smukee kitchen	26.06.2020	China

The International Agency for Research on Cancer and the World Health Organization (IARC/WHO) have concluded that PAAs are potentially harmful human health, cause cancer and bring about other adverse consequences.

PAAs are regarded as toxic compounds and classified as mutagenic, cancerogenic, or likely cancerogenic factors for people (Aznar et al. 2009, Ripa et al. 2014, Campanella et al. 2015, Yavuz et al. 2016). There are claims in the literature that PAAs showcase genotoxic, cancerogenic and allergenic properties (Trier et al. 2010, Shahrestani et al. 2018). Moreover, 2,4-toluenediamine (2,4-TDA), which is classified as a PAA, has a toxic effect on spermatogenesis, as well as the production and activity of androgens (Thysen et al. 1985). Studies carried out on animals exposed to 2,4-toluenediamine (2,4-TDA) showed that it can also be a cancerogenic factor to people (Persson et al. 1993, Shanmungam et al. 2001, Sielken et al. 2012, Rudel et al. 2014).

Azodyes, which are used to dye various products which come in contact with food, may contain aromatic amines whose cancerogenic activity is either clinically proven or under debate (Ahlström et al. 2005). Noteworthy, some azodyes may be extremely toxic and mutagenic (Bafana et al. 2011).

There is a list shared by the EU countries which includes a register of aromatic amines originating from the breakdown of azodyes whose concentration should be under constant monitoring due to their cancerogenic pro-

Table 2

Amines, their abbreviated name, CAS number, IARC classification group

Amines	Abbreviated name	CAS number	IARC classification group
Benzidine	BNZ	92-87-5	1
2-Naphthylamine	2-NA	91-59-8	1
4-Aminobiphenyl	4-ABP	92-67-1	1
4.4-Methylene-bis-(2-chloroaniline)		101-14-4	1
o-Toluidine	o-T	95-53-4	1
4-Chloro-o-toluidine	4-CoT	95-69-2	2A
4,4-Oxydianiline	4,4-DPE	101-80-4	2B
o-Tolidine		119-93-7	2B
3,3-Dimethylbenzidine	3,3-DMB	119-93-7	2B
p-Chloroaniline	4-CA	106-47-8	2B
2,4-Diaminoanisole		615-05-4	2B
4-Methoxy-m-phenylenediamine	4-M-mPDA	615-05-4	2B
4,4′-Methylene-bis-(2-methylaniline)		838-88-0	2B
4,4-Methylenedi-o-toluidine	4,4-MDoT	838-88-0	2B
4,4′-Thiodianiline	4,4´-thioANL	139-65-1	2B
o-Anisidine	o-ASD	90-04-0	2B
2,4-Toluenediamine	2,4-TDA	95-80-7	2B
4-Methyl-m-phenylenediamine		95-80-7	2B
3.3-Dichlorobenzidine		91-94-1	2B
3,3´-dimethylbenzidine	3,3´-DMB	119-93-7	2B
4,4´-diaminodiphenyl sulfide		139-65-1	2B
p-Aminoazobenzene		60-09-3	2B
o-Aminoazotoluene		97-56-3	2B

IARC classification groups: 1 – carcinogenic to humans; 2A – probably carcinogenic to humans; 2B – possibly carcinogenic to humans.

perties. The detectable amount of those analytes in final products or their dyed elements which come in direct contact with the skin or lips should not exceed 30 ppm (Directive 2002, Commission Regulation 2009).

Table 2 presents a selection of compounds classified as PAAs, which are established as or suspected to be cancerogenic to people (Mortensen et al. 2005, Aznar et al. 2009, Lambertini et al. 2014, Perez et al. 2019).

CONCLUSIONS

One of the biggest problems related to the safety of food is the migration of undesirable chemical substances from materials designated to come in contact with food, in particular food packaging.

The production of articles coming in contact with food involves the use of a variety of chemical substances, at the stage of production as well as subsequent processing. Migrating chemical compounds may lead to the pollution and contamination of food.

There is evidence confirming the threat of chemical substance release to food products. If such a product is food itself, migrating chemical compounds may not just cause changes to the smell and taste, but can also lead to the pollution and contamination of the packaged food.

The control and measurement of PAA migration from products and food packaging materials alike are some of the most significant issues of the food sector, especially for producers and food processors. Therefore, even the identification of trace levels of chemical substances from the production process has to be under strict control.

As far as public health is concerned, food safety in the broad sense of the term ought to go beyond the improvement of nutritional profiles, and therefore include regular monitoring, supervision and execution of regulations regarding food products as well as the quality and chemical composition of food contact products with the aim of ameliorating the general welfare and preventing diseases.

Conflict of interest: none declared.

REFERENCES

Ahlström L.H., Eskilsson C.S., Björklund E. 2005. *Determination of banned azo dyes in consumer goods*. Trends Analyt Chem., 24(1): 49-56. DOI:10.1016/j.trac.2004.09.004

Aznar M., Canellas E., Nerín C. 2009. *Quantitative determination of 22 primary aromatic amines by cation-exchange solid-phase extraction and liquid chromatography-mass spectrometry*. J Chromatogr. A., 1216(27): 5176-5181. DOI: 10.1016/j.chroma.2009.04.096

Bafana A., Devi S.S., Chakrabarti T. 2011. *Azo dyes: past, present and the future*. Environ Rev., 19(NA): 350-371. DOI: 10.1139/a11-018

Campanella G., Ghaani M., Quetti G., Farris S. 2015. *On the origin of primary aromatic amines in food packaging materials*. Trends Food Sci Technol., 46(1): 137-143. DOI: 10.1016/j.tifs.2015.09.002

Ciecierska M. 2014. *Evaluation of level of consumer awareness in migration of undesirable chemicals to food from food packaging and food contact materials*. Nauki Inż. Technol., 4(15): 23-30. (in Polish) DOI: 10.15611/nit.2014.4.02

Costa M.C., Goumperis T., Andersson W., Badiola J., Ooms W., Pongolini S., Saegerman C., Jurkovic M., Tuominen P., Tsigarida E., Steinwider J., Holzl C., Mikushinska N., Gross-Boskovic A., Kanari P., Christodoulidou M., Babicka L., Korsgaard H., Pesonen S., Fillet A.M., Foures F., Lohman M., Luber P., Szabo M., Cseh J., Noteborn H.P.J.M.,

Færden K., Fulke Å., Trnovec T., Ilback N.G., Andersson T., Donohoe T., Merten C., Robinson T. 2017. *Risk identification in food safety: Strategy and outcomes of the EFSA emerging risks exchange network (EREN), 2010-2014*. Food Control., 73: 255-264. DOI: 10.1016/j.foodcont.2016.04.045

Commission Directive 2007/19/EC of 30 March 2007 *amending Directive 2002/72/EC relating to plastic materials and articles intended to come into contact with food and Council Directive 85/572/EEC laying down the list of simulants to be used for testing migration of constituents of plastic materials and articles intended to come into contact with foodstuffs* (Text with EEA relevance) *OJ L 91, 31.3.2007, p. 17-36. https://eur-lex.europa.eu/legal-content//EN/TXT/?uri=CELEX%3A32007L0019*

Commission Regulation **(**EC) No 552/2009 of 22 June 2009 *amending Regulation (EC) No 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) as regards Annex XVII* (Text with EEA relevance). OJ L 164, 26.6.2009, p. 7-31. https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex%3A32009R0552

Commission Regulation **(**EU) No 10/2011 of 14 January 2011 on *plastic materials and articles intended to come into contact with food* Text with EEA relevance. OJ L 12, 15.1.2011, p. 1-89. http://data.europa.eu/eli/reg/2011/10/oj

Ćwiek-Ludwicka K., Pawlicka M., Starski A., Andrzej Starski, Półtorak H., Karłowski K. 2011. *Studies on primary aromatic amines (PAAs) migration from multi-layer plastic food packaging by HPLC method*. Rocz Panstw Zakl Hig., 62: 371-375. (in Polish) http://yadda.icm.edu.pl/yadda/element/bwmeta1.element.dl-catalog-bbab0b57-c586-4a04-ad1b-f870dab30392

Directive 2002/61/EC of the European Parliament and of the Council of 19 July 2002 *amending for the nineteenth time Council Directive 76/769/EEC relating to restrictions on the marketing and use of certain dangerous substances and preparations (azocolourants)*. OJ L 243, 11.9.2002, p. 15-18. http://data.europa.eu/eli/dir/2002/61/oj

Doe J.E., Hoffmann H.D. 1995. *Toluene Diisocyanate: an assessment of carcinogenic risk following oral and inhalation exposure*. Toxicol Ind Health, 11(1): 13-32. DOI: 10.1177/074823379501100102

Eto K. 2000. *Minamata disease*. Neuropathology, 20(s1): 14-19. DOI: 10.1046/j.1440-1789.2000.00295.x

EFSA. Technical Report 2017. *Administrative Guidance for the preparation of applications for the safety assessment of substances to be used in plastic Food Contact Materials*. EFSA supporting publication EN-1224. 41 pp. DOI:10.2903/sp.efsa.2017.EN-1224

El-Nezami H., Tam P.K., Chan Y., Lau A.S., Leung F.C., Chen S.F., Lan L.C., Wang M.F. 2013. *Impact of melamine-tainted milk on foetal kidneys and disease development later in life*. Hong Kong Med J., 19(Suppl), 8: 34-38. https://core.ac.uk/download/pdf/38041084.pdf

European Commission. RASFF Portal, 2021 https://webgate.ec.europa.eu/rasff-window/portal/?event=SearchByKeyword&StartRow=1 (access on 28.03.2021 r.)

Favaro Perez M.Â., Padula M., Moitinho D., Grespan Bottoli C.B. 2019. *Primary aromatic amines in kitchenware: determination by liquid chromatography-tandem mass spectrometry*. J Chromatogr A., 1602(17): 217-227. DOI:10.1016/j.chroma.2019.05.019

Fung F., Wang H.S., Menon S. 2018. *Food safety in the 21st century*. Biomed J., 41(2): 88-95. DOI: 10.1016/j.bj.2018.03.003

GIS. 2021. *Public warning about food*. (in Polish) https://www.gov.pl/web/gis/ostrzezenia

Godfray H.C, Beddington J.R, Crute I.R., Haddad L., Lawrence D., Muir J.F., Pretty J., Robinson S., Thomas S.M., Toulmin C. 2010. *Food security: The challenge of feeding 9 billion people*. Science, 327: 812-818. DOI: 10.1126/science.1185383

Geueke B., Muncke J. 2017. *Substances of very high concern in food contact materials: Migration and regulatory background*. Packag Technol Sci., 31(12): 757-769. DOI: 10.1002//pts.2288

Ikeda M., Ezaki T., Tsukahara T., Moriguchi J. 2004. *Dietary cadmium intake in polluted and non-polluted areas in Japan in the past and in the present*. Int Arch Occup Environ Health, 77(4): 227-234. DOI: 10.1007/s00420-003-0499-5

Lambertini F., Di Lallo V., Catellani D., Mattarozzi M., Careri M., Suman M. 2014. *Reliable liquid chromatography-mass spectrometry method for investigation of primary aromatic amines migration from food packaging and during industrial curing of multilayer plastic laminates*. J Mass Spectrom., 49(9): 870–877. DOI: 10.1002/jms.3436

Latos M., Masek A. , Zaborski M. 2017. *Migration of a modifying agent from polymer packaging materials*. Przetwórstwo Tworzyw, 23(178): 364-369. (in Polish) http://yadda.icm.edu.pl/ /baztech/element/bwmeta1.element.baztech-5eb2d3e5-8380-4c35-aa98-3d830b330a82

Li M.C., Tsai P.C., Chen P.C., Hsieh C.J., Leon Guo Y.L., Rogan W.J. 2013. *Mortality after exposure to polychlorinated biphenyls and dibenzofurans: 30 years after the "Yucheng Accident"*. Environ Res., 120: 71-75. DOI: 10.1016/j.envres.2012.09.003

Li Y., Li Ch., Xiao D., Liang F., Chen Z., Chen X., Sun X., Li Y. 2013. *Determination of migration of 25 primary aromatic amines from food contact plastic materials by gas chromatography-mass spectrometry*. Chin J Chromatogr., 31(1): 46-52. DOI: 10.3724SP.J.1123. 2012.08055

Marchildon K. 2011. *Polyamides – still strong after seventy years*. Macromol React Eng, 5(1): 22-54. DOI: 10.1002/mren.201000017

Mattarozzi M., Lambertini F., Suman M., Careri M. 2013. *Liquid chromatography-full scan-high resolution mass spectrometry-based method towards the comprehensive analysis of migration of primary aromatic amines from food packaging*. J Chromatogr A., 1320:96-102. DOI: 10.1016/j.chroma.2013.10.063

McCall E., Keegan J., Foley B. 2012. *Primary aromatic amine migration from polyamide kitchen utensils: method development and product testing*. Food Addit Contam, Part A, 29(1): 149-160. DOI: 10.1080/19440049.2011.615031

Merkel S., Kappenstein O., Sander S., Weyer J., Richter S., Pfaff K., Luch, A. 2018. *Transfer of primary aromatic amines from coloured paper napkins into four different food matrices and into cold water extracts*. Food Addit Contam, Part A, 35(6), 1223-1229. DOI: 10.1080/ /19440049.2018.1463567

Mortensen S.K., Trier X.T., Foverskov A., Petersen J.H. 2005. *Specific determination of 20 primary aromatic amines in aqueous food simulants by liquid chromatography-electrospray ionization-tandem mass spectrometry*. J Chromatogr, Part A, 1091(1-2): 40-50. DOI: 10.1016/j.chroma.2005.07.026

Nowotyńska I., Grabowska G., Zdeb M. 2018. *Comparative analysis of selected plastic packaging*. Autobusy – Technika, Eksploatacja, Systemy Transportowe. 19(12): 936-940. (in Polish) DOI: 10.24136/atest.2018.527

Paseiro-Cerrato R., Noonan G.O., Begley T.H. 2014. *Development of a rapid screening method to determine primary aromatic amines in kitchen utensils using direct analysis in real time mass spectrometry (DART-MS)*. Food Addit Contam, Part A, 31(3): 537-545. DOI: 10.1080/ /19440049.2013.867366

Pawlicka M., Mazańska M., Postupolski J. 2015. *Formaldehyde and other potentially carcinogenic substances in food packaging*. Przem. Spoż., 69(1): 30-31. (in Polish) DOI: 10.15199/ /65.2015.1.6

Perez M.Â.F., Padula M., Moitinho D., Bottoli C.B.G. 2019. *Primary aromatic amines in kitchenware: determination by liquid chromatography-tandem mass spectrometry*. J Chromatogr, Part A, DOI: 10.1016/j.chroma.2019.05.019

Persson P., Adamsson M., Dalene M., Skarping G., Hagmar L. 1993. *Determination of occupational exposure to toluenediisocyanate by biological monitoring in urine and plasma by gas chromatography-mass spectrometry*. Br J Ind Med., 50:1 111-1118. https://www.ncbi.nlm. nih.gov/pmc/articles/PMC1061334/pdf/brjindmed00012-0055.pdf

Pezo D., Fedeli M., Bosetti O., Nerín, C. 2012. *Aromatic amines from polyurethane adhesives in food packaging: The challenge of identification and pattern recognition using Quadrupole--Time of Flight-Mass Spectrometry E*. Anal. Chim. Acta, 756: 49-59. DOI: 10.1016/j.aca.2012.10.031

Poças M.F., Hogg T. 2007. *Exposure assessment of chemicals from packaging materials in foods: a review*. Trends Food Sci Technol., 18(4): 219-230. DOI: 10.1016/j.tifs.2006.12.008

Ripa L, Mee C, Sjö P, Shamovsky I. 2014. *Theoretical studies of the mechanism of N-hydroxylation of primary aromatic amines by cytochrome P450 1A2: radicaloid or anionic?* Chem Res Toxicol., 27(2): 265-78. DOI: 10.1021/tx400376u

Regulation (EC) No 1935/2004 of the *European Parliament and of the Council of 27 October 2004 on materials and articles intended to come into contact with food and repealing Directives 80/590/EEC and 89/109/EEC*. OJ L 338, 13.11.2004, p. 4-17. https://eur-lex.europa.eu//legal-content/EN/TXT/?uri=celex%3A32004R1935

Rubio L., Sanllorente S., Sarabia L.A., Ortiz, M.C. 2014. *Optimization of a headspace solid-phase microextraction and gas chromatography/mass spectrometry procedure for the determination of aromatic amines in water and in polyamide spoons*. Chemometr Intell Lab Syst., 133: 121-135. DOI: 10.1016/j.chemolab.2014.01.013

Rudel R.A., Ackerman J.M., Attfield K.R., Brody J.G. 2014. *New exposure biomarkers as tools for breast cancer epidemiology, biomonitoring, and prevention: a systematic approach based on animal evidence*. Environ Health Perspect., 122(9): 881-895. DOI: 10.1289/ehp.1307455

Sanchis Y., Coscollà C., Yusà V. 2019. *Comprehensive analysis of photoinitiators and primary aromatic amines in food contact materials using liquid chromatography High-Resolution Mass Spectrometry*. Talanta., 191: 109-118. DOI: 10.1016/j.talanta.2018.08.047

Sanllorente S., Sarabia L.A., Ortiz M.C. 2016. *Migration kinetics of primary aromatic amines from polyamide kitchenware: Easy and fast screening procedure using fluorescence*. Talanta, 160: 46-55. DOI:10.1016/j.talanta.2016.06.060

Sendón R., Bustos J., Sánchez J.J., Paseiro P., Cirugeda M.E. 2010. *Validation of a liquid chromatography-mass spectrometry method for determining the migration of primary aromatic amines from cooking utensils and its application to actual samples*. Food Addit Contam, Part A., 27(1): 107-117. DOI: 10.1080/02652030903225781

Shahrestani M., Tehrani M.S., Shoeibi S., Azar P.A., Husain S.W. 2018. *Comparison between different extraction methods for determination of primary aromatic amines in food simulant*. J Anal Methods Chem, 1651629. DOI: 10.1155/2018/1651629

Shanmungam K., Subrahamanyam S., Tarakad S.V., Kodandapani N., Stanly D.F. 2001. *2,4-toluene diamines. their carcinogenicity, biodegradation, analytical techniques and an approach towards development of biosensors*. Anal Sci., 17(12): 1369-1374. DOI: 10.2116/analsci.17.1369

Shimohata T., Hirota K., Takahashi H., Nishizawa M. 2015. *Clinical aspects of the Niigata Minamata disease*. Brain Nerve., 67(1): 31-8. DOI: 10.11477/mf.1416200084

Sielken R.L. Jr, Bretzlaff R.S., Valdez-Flores C., Parod R. 2012. *Statistical comparison of carcinogenic effects and dose-response relationships in rats and mice for 2,4-toluene diamine to those ascribed to toluene diisocyanate*. Hum Ecol Risk Assess., 18(6): 1315-1337. DOI: 10.1080/10807039.2012.722853

The Law of August 25, 2006 on *food and nutrition safety*. Dz. U. 2006 nr 171 poz. 1225 ze zm. (in Polish) https://isap.sejm.gov.pl/isap.nsf/DocDetails.xsp?id=WDU20061711225

Thysen B., Bloch E., Varma, S.K. 1985. *Reproductive toxicity of 2,4-toluenediamine in the rat. 2. Spermatogenic and hormonal effects*. J Toxicol Environ Health, 16(6): 763-769. DOI: 10.1080/15287398509530787

Trier X., Okholm B., Foverskov A., Binderup M., Petersen J. 2010. *Primary aromatic amines (PAAs) in black nylon and other food-contact materials, 2004-2009*. Part A. *Chemistry,*

analysis, control, exposure and risk assessment. Food Addit Contam., 27: 1325-1335. DOI: 10.1080/19440049.2010.487500

Ochwanowska E., Czarny-Działak M., Żeber-Dzikowska I., Wójtowicz B., Gworek B., Król H., Dziechciaż M., Szpringer M., Chmielewski J. 2019. *Chemicals in food as a health threat*. Przem Chem., 99(10): 1614-1618. (in Polish) DOI: 10.15199/62.2019.10.17

Yavuz O., Valzacchi S., Hoekstra E., Simoneau C. 2016. *Determination of primary aromatic amines in cold water extract of coloured paper napkin samples by liquid chromatography--tandem mass spectrometry*. Food Addit Contam, Part A, 33(6): 1072-9. DOI: 10.1080/ /19440049.2016.1184493

Xiao X., Wang J., Yang J., Liu T., Chen T., He J., Deng H., Gao Q. 2013.*Rapid analysis of 28 primary aromatic amines in aqueous food simulants by high performance liquid chromatography-tandem mass spectrometry*. Chin J Chromatogr., 31(1): 38-45. DOI: 10.3724/ /sp.j.1123.2012.10028