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LETTER TO THE EDITOR

Questionable information on poisonings by alcohol surrogates

Sergei JARGIN
Peoples' Friendship University of Russia, Moscow, Russia

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DEAR EDITOR,

Herewith I would like to submit for publication a letter to the Editor with reference to the article:
Asiedu-Gyekye IJ, Mahmood AS, Awortwe C, Nyarko AK. Toxicological assessment of polyhexamethylene biguanide for water treatment. Interdisciplinary Toxicolology 2015; **8**: 193–202.

KEY WORDS: ethanol; methanol; polyhexamethylene guanidine; PHMG; toxic hepatitis

During the anti-alcohol campaign in the former Soviet Union (1985-1988), many distilleries producing alcoholic beverages of standard quality were closed and dismantled. Due to restricted sales, many people were drinking industrial liquid preparations, as window cleansing, lotions, etc. The alcohol consumption increased after the campaign (Jargin, 2010, 2016). At the same time, technical alcohol (synthetic and cellulosic) met no demand from the stagnating industry. Official permissions to use alcohol from non-edible raw materials for the production of beverages were issued during the 1990s (Nemtsov, 2010; Nuzhnyi *et al.*, 2016). The permissions have later been revoked but, on the background of disregard for some laws and regulations, the use of technical alcohol has continued by some manufacturers. It was repeatedly demonstrated in animal experiments that synthetic and cellulosic alcohol are more toxic than alcohol from edible raw materials. Later on, purified synthetic and cellulosic alcohol were reported to comply with requirements for beverage alcohol (Nuzhnyi *et al.* 2016). Note that animal experiments may overestimate toxicity of alcohol produced by natural fermentation from edible raw materials in humans compared to synthetic and cellulosic ethanol. Milleniums of adaptation of certain human populations to alcohol included adaptation to chemical by-products of natural fermentation. Innovative methods of alcohol manufacturing are accompanied by a generation of new by-products, adaptation to which has not developed yet.

Diluted technical alcohol has been sold in vodka bottles through legally operating shops and eateries, added to beer, wine and other beverages. Following abolition of the state alcohol monopoly in 1992, the country was flooded by low-quality alcoholic beverages. The quality of sold alcohol seems to have improved since approximately the last decade. For more details and references see Jargin, 2010, 2016. Some publications create the impression that consumers deliberately purchase surrogates for drinking (Khaltourina & Korotayev, 2016). According to our observations and generally known facts, drinking of technical liquids and lotions has decreased abruptly after the end of the anti-alcohol campaign in 1989, when vodka, beer and other beverages have become easily available and were relatively cheap. The only major exceptions are alcohol-containing liquids from the drug store. Some people go to the pharmacy not because of the lower price but as they hope to obtain quality alcohol, i.e. better purified than vodka from the bottle store. Converted to absolute alcohol, the tinctures from pharmacies are currently more expensive than cheap vodka. Recently 77 lethal cases were reported from a mass poisoning in Irkutsk (December 2016). According to available information, the poisoning was caused by the bath lotion Boyaryshnik (Hawthorn) containing 93% ethyl alcohol, hawthorn extract, lemon oil, diethyl phthalate and glycerol, yet the chemical analysis has reportedly shown that the lotion contained methyl alcohol (RT News, 2016; Wikipedia, 2016). The poisoning has however been suspected to have been caused by hawthorn (Crataegus) tincture containing according to the label 70% ethanol. The hawthorn tincture is the most common form of medicinal alcohol

Correspondence address:
Dr. Sergei Jargin
Peoples' Friendship University of Russia
Clementovski per 6-82, 115184 Moscow, Russia.
TEL/FAX: 7-495-9516788 • E-MAIL: sjargin@mail.ru

consumed by drinkers in Russia (Monakhova *et al.*, 2011; Gil *et al.*, 2009). The author has found no information on Hawthorn Bath Lotion containing 93% of ethanol. There could have been misinformation intended to disguise the fact that methanol has been used as a cheap substitute for medicinal alcohol. Another mass poisoning occurred in several places of the Russian Federation in 2006, particularly in Siberia. The number of poisonings with marked jaundice during the period August-November 2006 was reported to have amounted to 12,611, including 1189 lethal cases, reportedly caused by the disinfectant Extrasept-1, containing 0.08-0.15% of diethyl phthalate and 0.1-0.14% of polyhexamethylene guanidine (PHMG) hydrochloride sold in vodka bottles (Luzhnikov, 2014; Ostapenko *et al.*, 2011). Actual figures are unknown. Cholestatic hepatitis with "a marked inflammatory component" was described in liver biopsies (Ostapenko *et al.*, 2011). Apart from PHMG, "chloride compounds", i.e. organochlorides have been discussed as possible causative factors (Khaltourina & Korotayev, 2016; Nuzhnyi *et al.*, 2010). The latter seems to be more probable as PHMG has no strong hepatotoxicity; its LD50, when administered orally, has been around 450 mg/kg for mice and 630 mg/kg for rats (Lachenmeier *et al.*, 2012) or somewhat higher, while the animals died with signs of injury to the nervous system (Asiedu-Gyekye *et al.*, 2014, 2015; Kondrashov, 1992; Tsisanova & Salomatin, 2010). Lung lesions due to PHMG used in household humidifiers have been reported (Kim *et al.*, 2016), but no reports on liver injury in humans have come to our attention.

The data on the 2006 mass poisoning have been cited in professional literature (Lachenmeier *et al.*, 2012; Asiedu-Gyekye *et al.*, 2015) and could have influenced conclusions. If the information on the poisonings in Russia has been incorrect, it can be misleading for the toxicity assessment of PHMG and the related substance polyhexamethylene biguanide (PHMB), both used as antimicrobial agents. The difference between LD50 estimates in rats for PHMG and PHMB by the same researchers in two consecutive studies was striking: 600 vs. 25.6 mg/kg (Asiedu-Gyekye *et al.*, 2014, 2015). Note that general toxicity of both substances is largely similar with LD50 values 500-600 mg/kg in rats when administered orally (Kim *et al.*, 2016). The question is whether the value 25.6 mg/kg (Asiedu-Gyekye *et al.*, 2015) could have resulted from added precaution due to information on the mass poisoning in Russia (Ostapenko *et al.*, 2011) cited by Asiedu-Gyekye *et al.* (2015). As for diethyl phthalate, its acute toxicity to mammals is low (Autian, 1973; Wams, 1987). Some phthalates can induce liver injury but it has not been confirmed when tested in primates and humans (NCEH, 2005). Further toxicological studies should test mixtures because combined action of ethanol, diethyl phthalate and PHMG may yield new results (Ostapenko *et al.*, 2011).

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