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Assessment of human health risk of cylindrospermopsin by consuming *Oryza sativa* (rice) from selected CKDu endemic areas in Sri Lanka

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The proliferation of toxic cyanobacterial blooms in freshwater bodies can seriously threaten human health. Many studies have been carried out on cyanotoxins in water sources, but studies on cyanotoxins in terrestrial plants are limited. Cyanotoxins in water sources can enter terrestrial plants when irrigated with cyanotoxin-contaminated water and cultivated in cyanotoxin-contaminated soil. As the main staple food in Sri Lanka, Oryza sativa (rice) is widely grown island-wide, mainly in the country's dry zone. The rice fields are irrigated with raw water from the reservoirs throughout their cultivation. Previous literature reported the presence of cyanotoxins, and potential cyanotoxinproducing cyanobacterial species in reservoirs in the dry zone in Sri Lanka. Moreover, cyanotoxins are hypothesized as one of the risk factors for chronic kidney disease of unknown aetiology (CKDu) in Sri Lanka. Cylindrospermopsin (CYN) is a cyanotoxin and negatively affects on several organs in the human body, including the kidneys. Therefore, the current study investigated CYN in O. sativa samples (n=102), including the most cultivated variants, samba (n=20), nadu (n=61), rathu kekulu (n=12) and keeri samba (n=9) collected from CKDu endemic Girandurukotte and Dehiattakandiya areas. As a control, rathu kekulu samples (n=22) were collected from CKDu non endemic Sewanagala area. CYN was extracted and analysed by high-performance liquid chromatography (HPLC) with reference to the CYN standard (SIGMA ALDRICH 32087). Estimated Daily Intake (EDI) of CYN was then calculated to determine the potential human health risk, for an adult by consumption of CYN-contaminated rice. Results of the HPLC analysis revealed that the mean ± SE values of CYN concentrations in samba, nadu, rathu kekulu, keeri samba rice from CKDu endemic areas and rathu kekulu from the control area were 6235.74 ± 1289.15 , 6821.44 ± 694.80 , 6538.66 ± 1797.81 , 3702.51 ± 1321.02 , and $3460.99 \pm 359.91 \ \mu g/kg$, respectively. Mean \pm SE of estimated daily intake when exposure to CYN via consumption of samba, nadu, rathu kekulu, keeri samba rice in CKDu endemic areas and rathu kekulu from the control area were 30.45±6.29, 33.31±3.39, 31.93±8.77, 18.08±6.44 and 16.90±1.75 µg/kg of body weight per day, respectively. All these values exceeded the provisional Tolerable Daily Intake (TDI) of CYN value established by the World Health Organization (0.03 µg/kg of body weight per day), which can pose a health risk to consumers. The present study revealed that the consumption of O. sativa in the studied areas has a potential risk of accumulation of CYN in the human body. However, it emphasized the importance of investigating the uptake of CYN into rice, in large sample sizes in the study areas.

Keywords: Cyanotoxins, Cylindrospermopsin, Estimated daily intake, Health risk, Oryza sativa

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