中文摘要

本研究以台灣砷盛行區域之西南沿海烏腳病地區與東北蘭陽平原之流行病學調查資料為基礎，利用 Weibull 模式建構砷暴露劑量、年齡與反應的關係，結合以生理為基礎的藥理動力學(PBPK)模式模擬人體代謝機制並探討飲水率所造成體內濃度變化，以評估飲用水含砷安全量。針對攝食西南沿海含砷養殖池之吳郭魚進行人體砷暴露健康風險評估，進而利用生物累積模式推求吳郭魚養殖池含砷安全量。生命階段之 PBPK 模式描述人體對主要代謝物種砷：As^{5+}，As^{3+}，MMA 及 DMA 之吸收、分佈、代謝與排除，並考量年齡生理狀態之潛在變化，強化攝食無機砷之風險評估。結果顯示膀胱癌、腎癌、尿道癌與肺癌之累積發生率，與年齡及劑量呈現明顯相關趨勢。以男性終生年齡 75 歲為例，膀胱癌為參考癌症，累積發生率 10^{-4} 下所推估飲用水含總砷安全量為 3.4 μg L^{-1}，但考量人體生理代謝機制與飲水率變化 (1.08－6.52 L d^{-1})時，飲用水含總砷安全量介於 1.9－10.2 μg L^{-1} 間，其所推估之累積發生率則為 2.84×10^{-5}－1.96×10^{-4} 間。根據攝食西南沿海地區含砷養殖池吳郭魚之健康風險評估，顯示布袋、義竹、北門及學甲區域風險均未超過 10^{-4}，而此地區 90%致癌風險落於 2.0×10^{-5} 範圍內。利用生物累積模式推求養殖吳郭魚水質顯示建議含無機砷安全量為 45 μg L^{-1}。本研究結合人體健康風險與環境評估步驟，整合流行病學與環境生物檢測研究，可提供建構環境風險管理架構以訂定規範與執行依據。

關鍵詞：砷；Weibull 模式；PBPK；飲用水標準；吳郭魚；風險評估；流行病學

Abstract

The purpose of this thesis is to evaluate a reasonable range of drinking water standard based on the arsenic epidemiological data in the southwestern Blackfoot disease-endemic area and northeastern Lanyang Plain in Taiwan. We present an integrated approach by linking the Weibull model-based dose-response profile and a physiologically based pharmacokinetic (PBPK) model to construct the interplay among arsenic exposure dose, age and response, and to model arsenic concentration varied with methylating activity and drinking water consumption rates. Furthermore, we use bioaccumulation model to establish a risk assessment for ingesting farmed tilapia in southwestern coast to estimate the pond water quality criteria. A life-stage PBPK model is used to describe the absorption, distribution, metabolism, and excretion of the four major metabolites: arsenate (As^{5+}), arsenite (As^{3+}), methylarsonic acid (MMA) and dimethylarsinic acid (DMA) in target tissue groups, considering the potential impact by physiologically life-stage differences. The results show that arsenic exposure dose, age and the cumulative incidence ratio of the bladder, kidney, urinary and lung cancers are correlated significantly. The safe arsenic drinking water standard is estimated to be 3.4 μg L^{-1} based on the index cancer (bladder cancer) with cumulative incidence ratio equals 10^{-4} for a life time 75-yr male. The standard concentration and cumulative incidence ratio range from 1.9 – 10.2 μg L^{-1} and 2.84×10^{-5} – 1.96×10^{-4}, respectively, which are varied with the drinking water consumption rates ranging from 1.08 – 6.52 L d^{-1}. The risk of ingesting farmed tiliapia are lower than 10^{-4} in Putai, Yichu, Paiman and Hsuehchia, and the average risk of 90% belows 2.0×10^{-5} in southwestern coast. The pond water standard of inorganic arsenic for farmed tilapia is estimated to be 45 μg L^{-1}. In conclusion, this study offers a environmental-risk-management framework to establish regulations and administrating process by linking epidemiological data and environmental bioassays.

Keywords：Arsenic; Weibull model; PBPK; Drinking water standard; Tilapia; Risk assessment; Epidemiology