C-1

LEMBAR
HASIL PENILAIAN SEJAWAT SEBIDANG ATAU *PEER REVIEW*
KARYA ILMIAH : JURNAL ILMIAH

Judul Artikel Ilmiah	:	Activation of interleukin-6 and -8 expressions by methylmercury in human U937 macrophages involves RelA and p50
Penulis Artikel Ilmiah	:	Megumi Yamamoto, Noureen Khan, **Muflihatul Muniroh**, Eriko Motomura, Rie Yanagisawa, Takami Matsuyama, Christoph F. A. Vogel
Status Pengusul	:	Penulis pertama/**penulis anggota**/penulis korespondensi
Identitas Jurnal Ilmiah	:	a. Nama Jurnal : Journal of Applied Toxicology
		b. ISSN : 10991263, 0260437X
		c. Nomor/Volume/Hal : Volume 37, pages 611-620
		d. Edisi (bulan/tahun) : Issue 5, 5 May 2017
		e. Penerbit : John Wiley and Sons Ltd
		f. Jumlah halaman : 10 halaman
		g. DOI artikel (Jika ada) : 10.1002/jat.3411
		h. Alamat web Jurnal : https://onlinelibrary.wiley.com/doi/abs/10.1002/jat.3411
		i. Terindeks di : SCOPUS (Q2); SJR 0,8

Kategori Publikasi Jurnal Ilmiah : (beri ✓ pada kategori yang tepat)
- [✓] Jurnal Ilmiah Internasional
- [ ] Jurnal Ilmiah Nasional Terakreditasi
- [ ] Jurnal Ilmiah Nasional tidak Terakreditasi

I. Hasil Penilaian *Peer Review* :

Komponen Yang Dinilai	Nilai Maksimal Karya Ilmiah (isikan di kolom yang sesuai)			Nilai Akhir Yang Diperoleh
	Internasional	Nasional Terakreditasi	Nasional tidak Terakreditasi	
	40			
a. Kelengkapan dan Kesesuaian unsur isi artikel(10%)	4			4.00
b. Ruang lingkup dan kedalaman pembahasan	12			11.00
c Kecukupan dan kemutahiran data/informasi dan metodologi (30%)	12			12.00
d. Kelengkapan unsur dan kualitas penerbit (30%)	12			11.00
Nilai Total = (100%)	**40**			**38.00**
Nilai pengusul =			**(40% x 38)/6 =**	**2.53**

KOMENTAR/ULASAN PEER REVIEW

Kelengkapan dan Kesesuaian Unsur	:	Struktur paper lengkap sesuai dengan original research article, menampilkan gambar yang informatif, reference style konsisten dan baik.
Ruang Lingkup dan Kedalaman Pembahasan	:	Dalam introduction dapat dipahami kepentingan melakukan penelitian ini, dan urgency serta manfaatnya. Namun general imformasi mengenai Minamata disease tidak diuraikan sehingga awam akan mengalami kesulitan.
Kecukupan & Kemutakhiran Data & Metodologi	:	Merupakan penelitian in vitro dengan menggunakan cell line. Metodologi lengkap dan menguraikan tahapan dan prosedur serta interpretasinya.
Kelengkapan Unsur dan Kualitas Penerbit	:	Journal of Applied Toxicology merupakan journal terindex scopus Q2 dengan SJR 0.8 diterbitkan oleh Wiley Online Library.

Semarang, 1-Oct-20
Penilai 1

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	40			
a. Kelengkapan dan Kesesuaian unsur isi artikel(10%)	4			4
b. Ruang lingkup dan kedalaman pembahasan	12			11
c Kecukupan dan kemutahiran data/informasi dan metodologi (30%)	12			11
d. Kelengkapan unsur dan kualitas penerbit (30%)	12			11
Nilai Total = (100%)	**40**			**37**
Nilai pengusul =			**(40% x 37)/6 =**	**2,47**

KOMENTAR/ULASAN PEER REVIEW

Kelengkapan dan Kesesuaian Unsur	:	Sistematika artikel lengkap, diuraikan dengan baik dalam setiap bagiannya.
Ruang Lingkup dan Kedalaman Pembahasan	:	Pembahasan diljelaskan secara mendalam, menampilkan gambar-gambar pendukung dan telah mencitasi hampir semua jurnal <10 tahun
Kecukupan & Kemutakhiran Data & Metodologi	:	Metode dijelaskan dengan lengkap dan material yang digunakan terukur jelas.
Kelengkapan Unsur dan Kualitas Penerbit	:	Jurnal diterbitkan oleh John Wiley and Sons Ltd, merupakan jurnal internasional bereputasi terindeks Scopus Q2 dengan nilai SJR 0.8

Semarang,
Penilai 2

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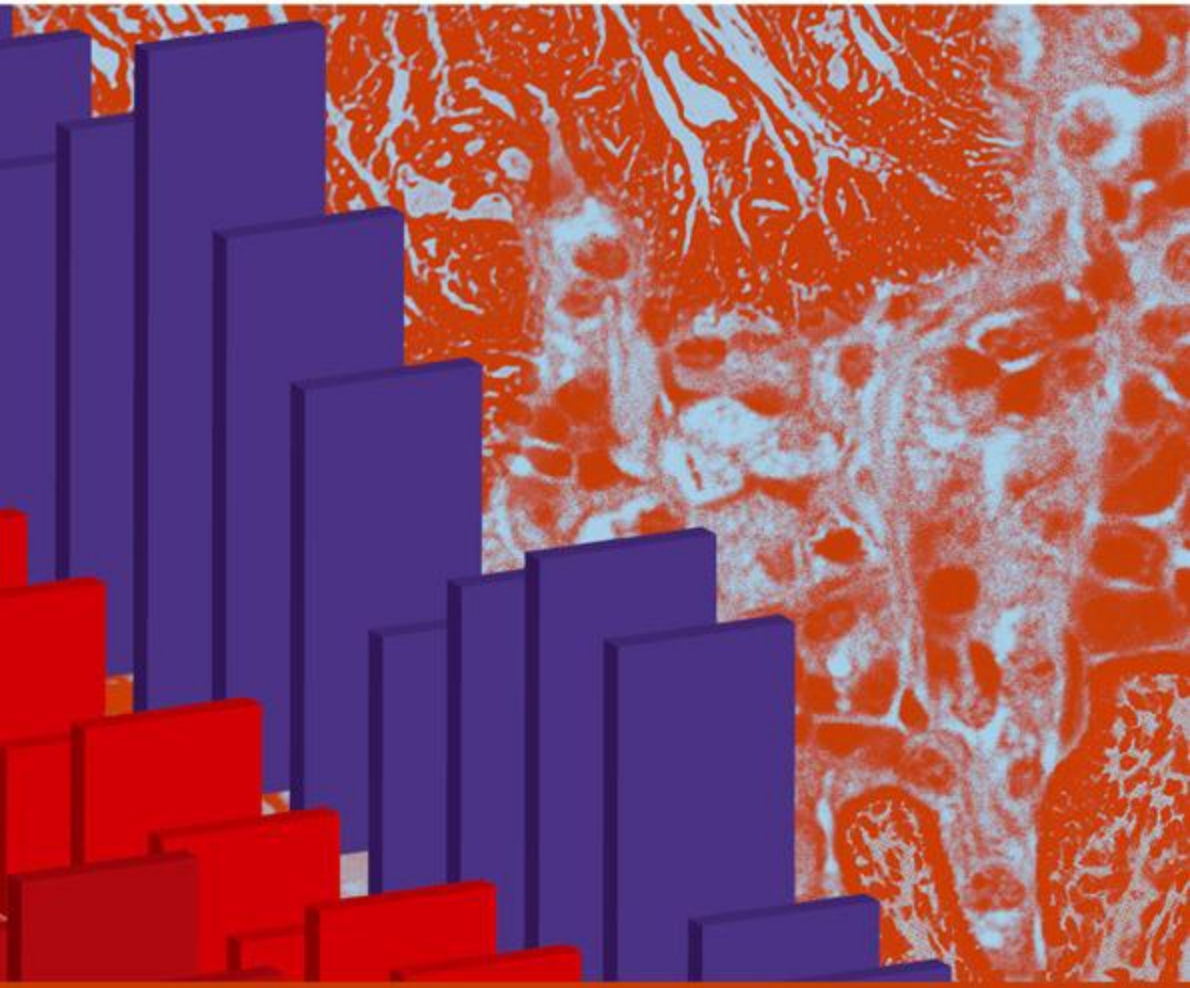
Volume 41 • Issue 3 • 2021
March 2021

Journal of Applied Toxicology



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Journal of Applied Toxicology

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Journal of Applied Toxicology

Aims & Scope

Journal of Applied Toxicology publishes reviews and research articles on mechanistic, fundamental and applied research relating to the toxicity of drugs and chemicals at the molecular, cellular, tissue, target organ and whole body level *in vivo* (by all routes of exposure) and *in vitro*/*ex vivo*. Focus is on toxicogenomics and proteomics, teratogenesis/developmental/reproductive toxicology, carcinogenesis, mutagenesis,pharmacokinetics, pharmacotoxicological and metabolic mechanisms, risk assessment, environmental toxicology and environmental health as applied to humans (including epidemiological studies).

In addition *Journal of Applied Toxicology* also publishes analytical and method development studies, mechanistic and molecular toxicology studies on novel or existing drugs and chemicals, addressing important or topical aspects of toxicology. Special emphasis is given to papers of clear relevance to human health and regulatory pharmaceutical/chemical toxicology.

Authors wishing to submit a manuscript on chemical weapons material's should contact the Editor-in-Chief first (see instructions for authors).

Volume 37 Number 5, May 2017

Review article

Research articles

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Journal of Applied Toxicology

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Journal of Applied Toxicology

Contents continued

Research article

Developmental toxicity of auranofin in zebrafish embryos

Xiao-Yan Gao, Kang Li, Ling-Ling Jiang, Ming-Fang He, Cun-Hai Pu, Dongzhou Kang, Jingjing Xie

First published: 04 November 2016 | https://doi.org/10.1002/jat.3410 | Citations: 13

Abstract

Auranofin (AF) is used in clinic for the treatment of rheumatoid arthritis, repurposing of AF as an anticancer drug has just finished a phase I/II clinical trial, but the developmental toxicity of AF remains obscure. This study focused on its developmental toxicity by using zebrafish embryos. Zebrafish embryos were exposed to different concentrations (1, 2.5, 5, 10 μM) of AF from 2 h post-fertilization (hpf) to 72 hpf. At 72 hpf, two major developmental defects caused by AF were found, namely severe pericardial edema and hypopigmentation, when embryos were exposed to concentrations higher than 2.5 μM. Biochemical detection of oxidative stress enzyme combined with expressions of a series of genes related to oxidative stress, cardiac, metal stress and pigment formation were subsequently tested. The superoxide dismutase activity was decreased while malondialdehyde content was accumulated by AF treatment. The expression of oxidative stress-related genes (*sod1*, *gpx1a*, *gst*), pigment-related genes (*mitfb*, *trp-1a*) and one metal stress-related gene *ctr1* were all decreased by AF exposure. The expressions of cardiac-related genes (*amhc*, *vmhc*) and one metal-related gene *hsp70* were found to be significantly upregulated by AF exposure. These findings indicated the potential developmental toxicity of AF on zebrafish early development.

(wileyonlinelibrary.com) DOI: 10.1002/jat.3412

Physiologically based pharmacokinetic model for ethyl *tertiary*-butyl ether and *tertiary*-butyl alcohol in rats: Contribution of binding to α2u–globulin in male rats and high-exposure nonlinear kinetics to toxicity and cancer outcomes

Susan J. Borghoff[a]*, Caroline Ring[a], Marcy I. Banton[b] and Teresa L. Leavens[c]

ABSTRACT: In cancer bioassays, inhalation, but not drinking water exposure to ethyl tertiary-butyl ether (ETBE), caused liver tumors in male rats, while tertiary-butyl alcohol (TBA), an ETBE metabolite, caused kidney tumors in male rats following exposure via drinking water. To understand the contribution of ETBE and TBA kinetics under varying exposure scenarios to these tumor responses, a physiologically based pharmacokinetic model was developed based on a previously published model for methyl tertiary-butyl ether, a structurally similar chemical, and verified against the literature and study report data. The model included ETBE and TBA binding to the male rat-specific protein α2u-globulin, which plays a role in the ETBE and TBA kidney responses observed in male rats. Metabolism of ETBE and TBA was described as a single, saturable pathway in the liver. The model predicted similar kidney $AUC_{0-\infty}$ for TBA for various exposure scenarios from ETBE and TBA cancer bioassays, supporting a male-rat-specific mode of action for TBA-induced kidney tumors. The model also predicted nonlinear kinetics at ETBE inhalation exposure concentrations above ~2000 ppm, based on blood $AUC_{0-\infty}$ for ETBE and TBA. The shift from linear to nonlinear kinetics at exposure concentrations below the concentration associated with liver tumors in rats (8000 ppm) suggests the mode of action for liver tumors operates under nonlinear kinetics following chronic exposure and is not relevant for assessing human risk.

Additional supporting information may be found in the online version of this article at the publisher's website.

Keywords: ethyl tertiary-butyl ether; PBPK model; tertiary-butyl alcohol; α2u- globulin; nephropathy

Introduction

Ethyl tertiary-butyl ether (ETBE, CAS 637-92-3) is used as a fuel oxygenate in oxygenated gasoline to improve combustion efficiency, allowing the gasoline to burn more completely and thereby reducing exhaust emissions. The technical characteristics of ETBE suggest that it is comparable to methyl tertiary-butyl ether (MTBE), a fuel oxygenate that had been more widely used until it was found to be mobile in groundwater. Based on concern for contamination of drinking-water sources (Malveda et al., 2009), MTBE was removed from the US market. However, the much lower water solubility of ETBE (26.7 g l^{-1}), compared to MTBE (42 g l^{-1}), is considered an advantage, because its mobility in groundwater will be lower than that of MTBE in the event of leakage from an underground storage tank (McGregor, 2007).

In the past 15 years, ETBE has not been used significantly as a gasoline additive in the USA and Europe. The US Geological Survey (2008) (USGS Circular, 1292) reported that ETBE was detected in less than 0.5% of public wells at concentrations of ~0.2 μg l^{-1}, with less frequent detection in domestic wells. In Japan, ETBE-blended gasoline has been used since 2007 (Eboli et al., 2011). The maximum atmospheric concentration of ETBE in the general environment is estimated to be ~0.0097 ppm (JPEC, 2008a). Eboli et al. (2011) reported that in Japan the geometric mean of 8 h time-weighted average exposure (TWA-8 h) to ETBE was 0.08 ppm (0.02–0.38 ppm) for 28 gas-station workers and 0.04 ppm (0.01–0.21 ppm) in two gasoline tanker truck drivers. None of the examined workers had a TWA-8 h exceeding the American Conference of Governmental Industrial Hygienists (ACGIH) threshold limit value (TLV) of 5 ppm, which was the threshold recommended by the ACGIH at the time the Eboli et al. (2011) study was published. The current occupational ACGIH TLV established for ETBE is now

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