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Editorial:

HIGHLIGHTS IN TOXICOLOGY

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Every year our cooperating journal, the *Archives of Toxicology*, publishes and analyzes its most cited articles. In 2009/2010 the most popular articles focussed on ethanol-induced liver damage, tea polyphenols as anti-carcinogens and concepts of dose-response modelling. To keep our readers informed about recent developments in toxicology we reproduce a table summarizing the take home messages of the most cited articles (Table; from: Bolt and Hengstler, 2011).

Table: Most cited articles in the Archives of Toxicology in 2009 and 2010

No.	Author	Take home message
1	Cederbaum et al. 2009	This is a comprehensive review explaining how ethanol-induced oxidative stress produces liver injury. Special emphasis is placed on ethanol-induced CYP2E1 induction.
2	Yang et al., 2009a	Polyphenolic compounds in tea are suggested to have anti-carcinogenic properties because they modulate carcinogen metabolism, prevent DNA damage and decrease oxidative stress. This review critically discusses possible anti-carcinogenic effects of tea polyphenols and summarises published evidence from animal models of carcinogenesis as well as epidemiological studies.
3	Calabrese, 2009a	The scientific community has shown preference to the threshold dose-response rather than the hormesis model. This is critically discussed, because the hormesis model may be superior in predicting responses in the low dose range.
4	Decker et al., 2009	Besides their role in detoxification, epoxide hydrolases are involved in signaling processes by metabolizing signaling lipids. This process seems to be relevant for the control of blood pressure, inflammation, proliferation and nociception.
5	Mahmud et al., 2009	Arsenic triggers suicidal erythrocyte death by increasing cytosolic Ca2+ concentrations. This may explain why environmental exposure to arsenic may lead to anemia.
6	Calabrese, 2009b	Linearity at low doses has become the basis for carcinogen risk assessment. The author criticizes this concept by re-visiting its foundations.
7	Furuyama et al., 2009	Ultrafine particles can be transported into the blood across the alveolar wall by endocytic pathways. In contrast, macrophages translocate not only ultrafine, but also fine particles from the lung to other organs.
8	Zheng et al., 2009	Oral exposure of mice to the environmental contaminant perfluorooctanesulfonate causes immunotoxic changes.

No.	Author	Take home message
9	Hu and Hu, 2009	Combined exposure of HepG2 cells to the environmental contaminants perfluorooctanoate and perfluorooctane sulfonate cause summation effects, but not synergistic or antagonistic effects.
10	Nakagawa et al., 2009	The designer drugs MDMA and derivatives are illegally used as recreational drugs. Unfortunately, some are hepatotoxic in humans. The present study shows that some amphetamine-derived drugs cause mitotoxicity and DNA damage in primary hepatocytes.
11	Kumar and Gill, 2009	Aluminium is the most widely distributed metal in the environment. This review describes mechanisms of aluminium-induced neurotoxicity, including mitochondrial stress and the accumulation of oxidized proteins.
12	Chen and Guo, 2009	Perfluoroalkyl acids show a site-specific binding to human serum albumin.
13	Grotto et al., 2009a	Selenium antagonizes the genotoxic and oxidative properties of low doses of methylmercury in rats.
14	Dewa et al., 2009	The benzimidazole anthelmintic oxfendazole causes oxidative stress in livers of rats which may contribute to tumor promotion.
15	Grotto et al., 2009b	Exposure of rats to low doses of methylmercury causes hypertension. Possible mechanisms are nitric oxide depletion and oxidative damage.
16	Kell, 2010	The author established a general concept of how poorly liganded iron is involved in the pathogenesis of several diseases, including Parkinson's, Huntington's and Alzheimer's disease. Possible interventions with iron chelators and antioxidants are discussed.
17	Sebai et al., 2009	Resveratrol protects from LPS-induced inflammation in rats.
18	Valdiglesias et al., 2010	Selenium may have anti-carcinogenic effects at low concentrations, but may be genotoxic and carcinogenic at higher concentrations. This comprehensive review summarizes the results of in vitro studies on mutagenicity, genotoxicity, cytotoxicity and DNA repair with selenium compounds from the last decades.
19	Pestka, 2010	The trichothecene mycotoxin deoxynivalenol (DON), also known as vomitoxin, is formed by the fungus Fusarium on wheat, barley and corn. This review gives an overview of human exposure, toxicity and mechanisms of action, including ribotoxic stress, compromised signal transduction, differentiation and proliferation.
20	Helal and Helal, 2009	Exogenously administered metallothionein protects against carmustine-induced pulmonary fibrosis in rats.
21	Schumann et al., 2009	A novel thermoluminescence-based technique for quantification of oxidative stress in mammalian cells or tissues has been established. In contrast to biochemical analysis this assay can be performed without extraction or specific preparation procedures by using directly collected material.
22	Wang et al., 2009a	Arsenic induces apoptosis in hepatocytes by the mitochondrial pathway.
23	Drobná et al., 2010	The relationship between potential arsenic transporters and cellular retention of inorganic arsenic and its methylated metabolites was analyzed. High MRP2 expression correlated with the production of dimethylarsenic metabolites.
24	Zhu et al., 2009	Exposure to the radioactive heavy metal depleted uranium can occur via inhalation of aerosols, ingestion and wounds. Implantation of depleted uranium into rats caused renal dysfunction.
25	Lu et al., 2009	Extracts of Antrodia camphorate cause apoptosis of HL 60 cells.

No.	Author	Take home message
26	Dong et al., 2009	Exposure of mice to perfluorooctanesulfonate at levels 50-fold higher than highly exposed humans affect immune functions.
27	Xie et al., 2010	The long-term quantitative biodistribution of silica nanoparticles was studied in mice. Silica nanoparticles accumulate in lung, liver and spleen because of endocytosis by macrophages.
28	Yang et al., 2009b	No significant differences in bisphenol A blood levels were obtained between breast cancer cases and controls.
29	Cervinková et al., 2009	Sensitive indicators of peroxidative damage induced by tert-butyl hydroperoxide in primary rat hepatocytes include a decrease in cytosolic glutathione and discharge of the mitochondrial membrane potential.
30	Stangherlin et al., 2009	Exposure of young rats to diphenyl ditelluride via maternal milk causes oxidative stress in the cerebral cortex and hippocampus.
31	Wang et al., 2009b	Lead acetate causes oxidative stress and apoptosis in primary cultures of rat proximal tubular cell.
32	Yan et al., 2009	Excessive intake of sodium fluoride may compromise the balance between bone formation and resorption leading to skeletal disease. This study showed that already relatively low fluoride concentrations may cause apoptosis of osteoblasts.
33	Rand et al., 2010	Damp building materials may host the anamorphic Trichocomaceae that form (1-3)-beta-d-glucan. This study demonstrates that (1-3)-beta-d-glucan causes an inflammation-associated gene expression pattern in mouse lungs.
34	Magdalan et al., 2009	This study describes the time course of alpha-amanitin toxicity in primary cultivated hepatocytes. Functional cells impairments, such as inhibition of protein and urea synthesis are followed by changes in ultrastructure (marginalization and condensation of nuclear chromatin) and necrosis as well as apoptosis.
35	Morfeld, 2009	In this letter, statistical analysis of an epidemiological study on the possible link between traffic-related atmospheric pollutants and birth weight is critically discussed.
36	Stapleton and Chan, 2009	The commonly used organophosphorus insecticide, chlorpyrifos alters expression of genes involved in neurological functions and development in the forebrain of rats at subtoxic doses.
37	Huang et al., 2009	A simple, fast and economic method for the simultaneous detection of aflatoxin B1 and ochratoxin A was established.
38	Xi et al., 2009	Exposure of pregnant rat dams and offspring pups to inorganic arsenite in drinking water at levels up to 100 mg/L affects learning and memory functions.
39	Zeng and Xie, 2009	Ethanol-induced steatosis represents a frequent health problem. Here, the role of the nuclear transcription factors PPAR alpha, SREBP-1 and the role of CYP2E1 are discussed.
40	Read et al., 2010	Phosphorylated butylcholinesterase and phosphorylated albumin are compared as biomarkers of organophosphorus exposure in guinea pigs.
41	Kawai et al., 2010	Piperonyl butoxide contributes to liver tumor promotion in mice by generation of reactive oxygen species.
42	Prigol et al., 2010	The organoselenium compound diphenyl diselenide caused seizure episodes in rat pups. The pups with the highest levels of diphenyl diselenide in liver and brain showed the shortest latency periods.
43	Angeli et al., 2009	The medicinal mushroom Agaricus blazei is discussed as an antimutagenic compound. It contains beta-glucan which antagonizes the genotoxic effect of benzo[a]pyrene in HepG2 cells.

No.	Author	Take home message
44	Ito et al., 2009	Fluoride-induced degranulation of rat exocrine pancreas cells represents a turning point from autophagy to apoptosis.
45	Sanchez et al., 2009	Colombostatin, a novel disintegrin, was isolated from the venom of the South American snake, Bothrops colombiensis. It was shown to inhibit platelet aggregation, and thus represents a drug candidate for the treatment of thrombotic diseases.
46	Kesarwani et al., 2009	An association between a GSTM3 intron 6 variant and prostate cancer risk was observed in a North Indian case control study.
47	Sidiropoulou et al., 2009	Diazinon oxon is a major in vivo metabolite of the phosphorothionate insecticide diazinon, which affects the differentiation of neuroblastoma cells in vitro.
48	Rizzi et al., 2009	Matrix metalloproteinase-2 plays a role in lead-induced hypertension.
49	Heng et al., 2009	This minireview discusses possibilities and limitations of using induced pluripotency stem cells in toxicity testing.
50	Shimizu et al., 2009	A glutathione-depleted mouse model was introduced to identify amodiaquine as an idiosyncratic hepatotoxic compound.

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