Most cited articles: ethanol-induced hepatotoxicity, anticarcinogenic effects of polyphenolic compounds in tea, dose–response modeling, novel roles of epoxide hydrolases and arsenic-induced suicidal erythrocyte death

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Every year, the editors of the Archives of Toxicology review the most cited articles from the previous 2 years (Table 1). This year, topping the most cited list (51 citations) is a comprehensive review by Arthur I. Cederbaum on the mechanisms of ethanol-induced liver injury, describing the contributions of oxidative stress and CYP2E1. The second most cited article also focuses on oxidative stress, but from a different perspective. Chung S. Yang describes how polyphenolic compounds in tea act as anticarcinogens. Besides their antioxidant properties, polyphenolic compounds prevent DNA damage and modulate carcinogen metabolism. Metabolic detoxification of carcinogens is also catalyzed by epoxide hydrolases. Martina Decker and colleagues contributed a comprehensive review, in which they describe that epoxide hydrolases play a role not only in detoxification but also in signaling processes by metabolizing lipids, thereby influencing blood pressure and inflammation. Edward J. Calabrese critically discusses why the hormesis model became marginalized in dose–response modeling. Finally, the most frequently cited original article was published by Hasan Mahmud and colleagues. They show that arsenic induces suicidal death of erythrocytes by increasing cytosolic Ca^{2+} concentrations, which may explain why environmental arsenic exposure causes anemia. Table 1 provides highlights of the most cited articles of 2009 and 2010.

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Table 1 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, b)	Polyphenolic compounds in tea are suggested to have anticarcinogenic properties because they modulate carcinogen metabolism, prevent DNA damage and decrease oxidative stress. This review critically discusses possible anticarcinogenic effects of tea polyphenols and summarizes published evidence from animal models of carcinogenesis as well as epidemiological studies
3	Calabrese (2009a, b)	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 Ca^{2+} concentrations. This may explain why environmental exposure to arsenic may lead to anemia
6	Calabrese (2009a, b)	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 perfluoro-octanesulfonate causes immunotoxic changes
9	Hu and Hu (2009)	Combined exposure of HepG2 cells to the environmental contaminants perfluorooctanoate and perfluorooctane sulfonate causes 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)	Aluminum is the most widely distributed metal in the environment. This review describes mechanisms of aluminum-induced neurotoxicity, including mitochondrial stress and the accumulation of oxidized proteins
12	Chen et al. (2009)	Perfluoroalkyl acids show a site-specific binding to human serum albumin
13	Grotto et al. (2009a, b)	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. (2009a, b)	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 anticarcinogenic 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 <i>Fusarium</i> 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 the 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, b)	Arsenic induces apoptosis in hepatocytes by the mitochondrial pathway
23	Drobná et al. (2009)	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

Table 1 continued

No.	Author	Take home message
25	Lu et al. (2009)	Extracts of <i>Antrodia camphorate</i> cause apoptosis of HL 60 cells
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. (2009a, b)	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. (2009a, b)	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 <i>Trichocomaceae</i> 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 <i>Agaricus blazei</i> is discussed as an antimutagenic compound. It contains beta-glucan that antagonizes the genotoxic effect of benzo[a]pyrene in HepG2 cells
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, <i>Bothrops colombiensis</i> . 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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