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Abstract Sifter: A literature informatics tool for chemical safety assessments

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Introduction

Identifying environmental chemicals that adversely affect human health or the environment requires assembling information from a wide variety of sources, including the millions of articles in the biomedical literature. Literature informatics approaches can help researchers make use of this literature in more effective ways. We have developed a freely available Excel-based tool called the Abstract Sifter to retrieve and triage articles and to visualize the literature landscape for a set of chemicals.

The tool is supplied with queries that facilitate exploration of mechanistic information by using the language of adverse outcome pathways (AOPs) and Key Characteristics of Carcinogens².

Defining mechanisms through PubMed queries

Toxicity type queries

Genetox	(dna/drug effects OR DNA Damage OR chromosome aberrations OR genotoxicity OR micronucleus OR DNA Repair OR mutageni	
Cancer	neoplasms or cancer	
ReproTox	(reproduction AND (toxicity OR abnormal OR adverse effects))	
NeuroTox	(neurotoxicity OR (Nervous system diseases and chemically induced) OR ((neurons OR brain OR behavior) AND drug effects)	
DevTox	(toxicity OR congenital abnormalities OR Prenatal Exposure Delayed Effects) AND (fetus OR embryo OR embryonic development)	
Skin sensitization	sensitization ("allergic" AND "contact" And dermatitis) OR Dermatitis, Allergic Contact[mh]	

			Events: Molecular Initiating Events (MIE) Key Events (KE) Adverse Outcomes (AO)				
			Sequence	Туре	Event ID	Title	Short name
aop43	1mie	(Vascular Endothelial Growth Factor Receptor-2 OR Vascular Endothelial Growth Facto		MIE	305	Inhibition, VegfR2	Inhibition, VegfR2
aop43	2ke	((angiogenesis OR vasculogenesis) AND (reduce OR inhibit)) OR (Neovascularization, I					
aop43	3ke	endothelium OR endothelial AND (damage OR impair OR impairment)	2	KE	28	Reduction, Angiogenesis	Reduction, Angiogenesis
			3	KE	110	Impairment, Endothelial network	Impairment, Endothelial network
aop44	4ke	Blood circulation AND (drug effects AND toxicity)	4	KE	298	Insufficiency, Vascular	Insufficiency, Vascular
aop43	5ao1	birth defects OR Congenital Abnormalities					
aop43	6ao2	(bone OR bone development OR calcification OR osteogenesis OR limb bud/drug effe	5	AO	1001	Increased, Developmental Defects	Increased, Developmental Defects

Aopwiki.org

Key Characteristics of Carcinogens queries

KCC1	Adducts	protein Adducts OR dna adducts OR epoxides OR quinones OR aldehydes
KCC2	2 DNA	(dna/drug effects OR DNA Damage OR chromosome aberrations OR genotoxicity OR micronucleus OR mutagenicity tests OR mutagens OR mut
KCC	DNA break/rep	(topoisomerase OR DNA Repair/drug effects OR double-strand break repair)
KCC4	Epigenetics	(DNA methylation OR histone modification OR Histone Code OR Chromatin Assembly and Disassembly OR microRNAs OR Epigenesis, Genetic)
KCC5	Oxidative stres	(oxidative stress OR reactive oxygen species OR mitochondria/drug effects)
KCC6	i Inflammation	(inflammation OR macrophages)
KCC7	7 Immunosuppre	(immunosuppressive OR immune system dysfunction)
KCC	Receptors	receptors AND (antagonism OR agonism OR drug effects)
KCC9	Cell immortaliz	(cell immortalization OR cell division OR hayflick limit OR Aging/genetics OR Cellular Senescence)
KCC1	.0 Proliferation	(cell proliferation OR cell death OR apoptosis OR Neovascularization, Pathologic)
Cano	er Cancer	(cancer OR neoplasms OR precancerous OR carcinogen OR carcinoma) AND (toxicity OR poisoning OR adverse effects)

Landscape view for three sample mechanistic reviews

Landscape Overview

The Landscape sheet lets the scientist build an overview of a literature domain by entering entity and subject matter queries.

Retrieve and sift the citations

The Main sheet is where the user can browse and use the novel sifting technology to find relevant articles

> Here's the Abstract What other sheet with t things can sifter terms colorized for easy reading

sends the user to the Abstract sheet.

bstract Sifter

Look here to see other useful and fun capabilities.

you do?

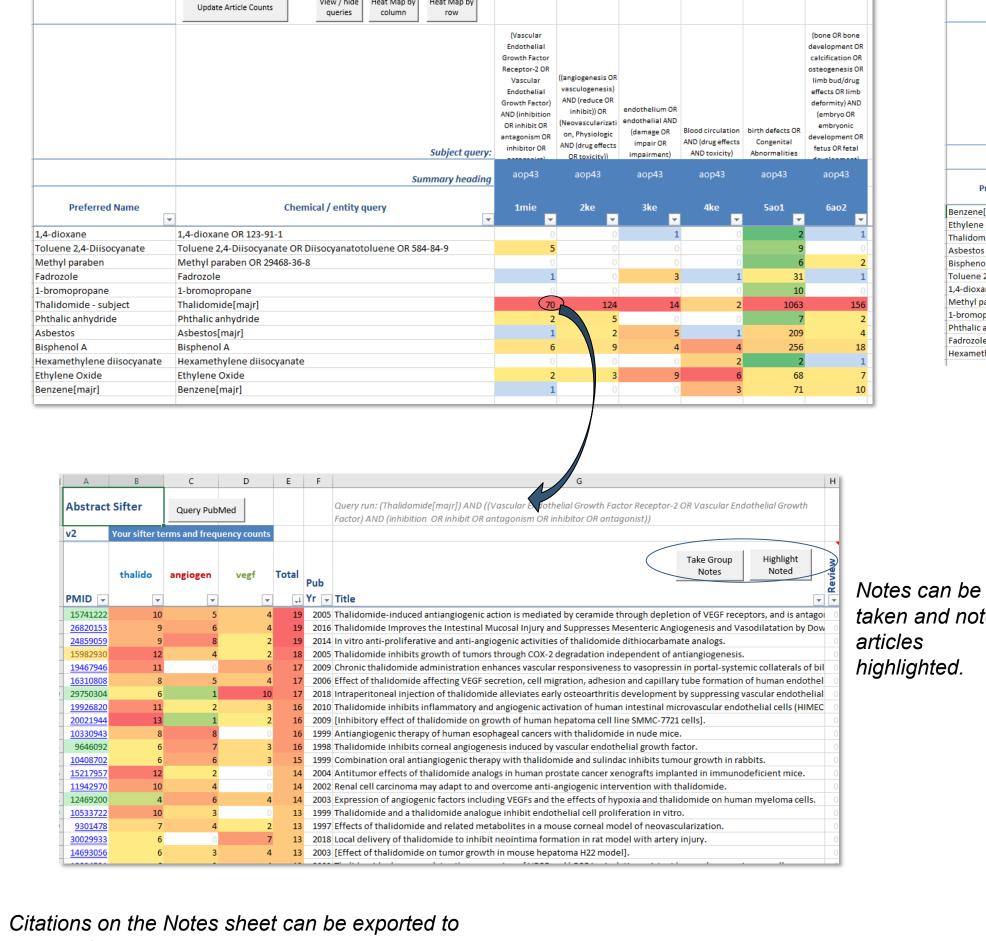
View / hide queries Heat Map by column row Preferred Name 1,4-dioxane OR 123-91-Phthalic anhydride Asbestos[majr] Modify the PubMed query and click on Submit. Benzene[majr] The numbers are article counts retrieved by the app Double-clicking on the article count retrieves the citations and sends them to the Main sheet To sift, enter terms or characters of interest here and let the Abstract Sifter count occurrences of the terms in the title and abstract. Then sort. Double-clicking on a row

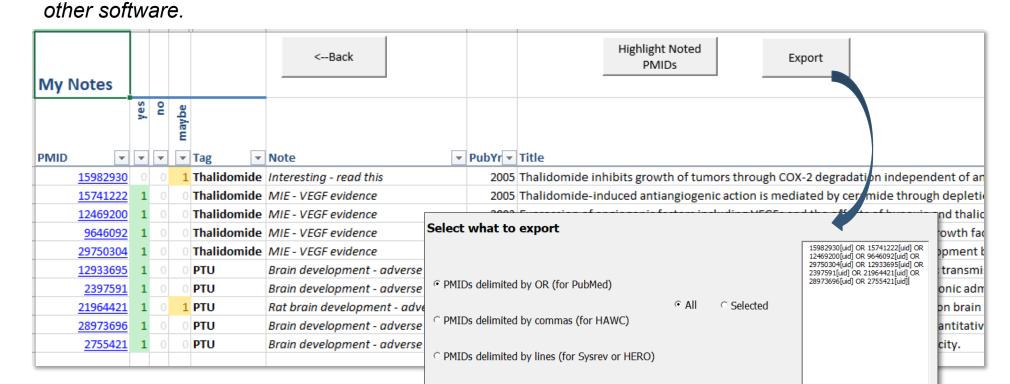
Toxicity Types

2008 Thirteen-week oral toxicity of 1,4-dioxane in rats and mice. 2016 INHIBITORY ACTIVITY OF PROTECTED EDIBLE PLANTS ON OXIDATIVE STRESS INDUCED BY ORAL 1,4-DIOXANE 2003 Functional characterization of alpha-adrenoceptors mediating pupillary dilation in rats. 1997 Characterization of alpha1-adrenoceptor subtypes in facilitation of rat spinal motoneuron activity

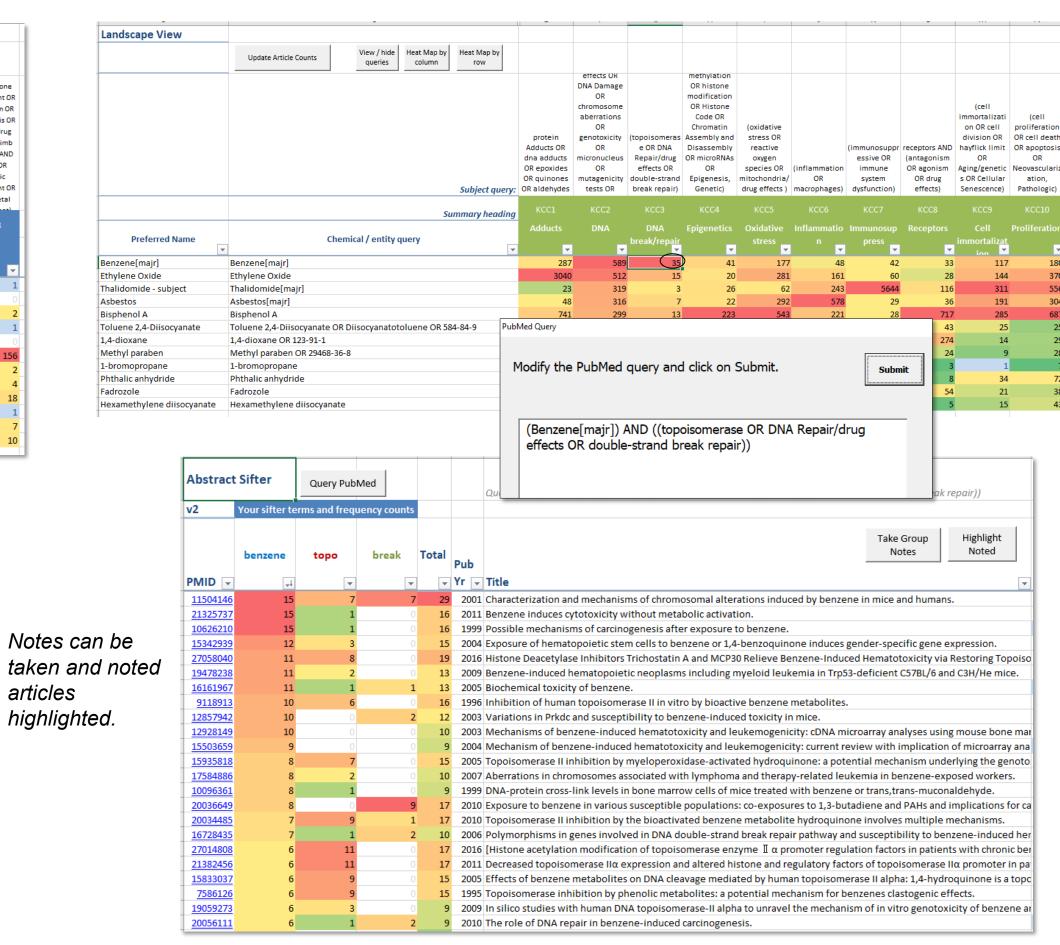
> Thirteen-week oral toxicity of 1,4-dioxane in rats and mice. Title and Thirteen-week oral toxicity of 1,4-dioxane in rats and mice. Abstract: Subchronic oral toxicity of 1,4-dioxane was examined by Abstract: administering 1,4-dioxane in drinking water at 6 different concentrations of 0 (control), 640, 1,600, 4,000, 10,000 or 25,000 ppm (wt/wt) dependently in rats and mice. A dose-dependent increase in the relative weights of kidney and lung was noted in rats and mice, while the relative liver weight was increased only in rats. Increases in plasma levels of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) and a decrease in plasma glucose were noted primarily in the rats and mice dosed 25,000 ppm. Histopathological examination revealed that 1.4-dioxane affected the upper and lower respiratory tracts, liver, kidneys and brain in rats, while only the the 1,4-dioxane-dosed rats and mice. The 1,4-dioxane-induced hepatic lesions were characterized by centrilobular swelling and necrosis in rats and mice and by glutathione S-transferase placental form (GST-P)-positive altered hepatocellular foci in rats, which are known as preneoplastic lesions. A no-observed-adverse-effect-level (NOAEL) was determined at 640 ppm for both rats and mice, since the nuclear enlargement in the nasal respiratory epithelium and the centrilobular swelling of hepatocytes in rats and the nuclear enlargement in the bronchial epithelium in mice were observed at 1,600 ppm. The NOAEL value corresponded to the estimated 1,4-dioxane intake of 52 mg/kg/day in rats and 170 mg/kg/day in mice

AOP 43: Vascular disruption





Key Characteristics of Carcinogens



Summary

The Abstract Sifter is a free, flexible literature retrieval tool that provides an overview of a complex literature landscape and the capability of focusing on mechanisms of toxicity. Available for download here:

ftp://newftp.epa.gov/COMPTOX/Sustainable_Chemistry_Data/Che mistry Dashboard/Abstract Sifter/

U.S. Environmental Protection Agency Office of Research and Development

This poster does not necessarily represent U.S. EPA policy.

References: 1) Baker N et al. F1000 Res. 2017 Dec 21;6. pii: Chem Inf Sci-2164. 2) Smith, et al. Environ Health Perspect. 2016 Jun;124(6):713-21.