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SysTox

AOP-helpFinder 2.0 results tutorial



AOP-helpFinder

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AOP-helpFinder 2.0 webserver: a tool for comprehensive analysis of the literature to support adverse outcome pathways development. 2023

Stressor-event search

stressor-event : output files

PMID	stressor	event	date	title
35670495	Benzene	liver cancer	2022	H2BZmacropa-NCS A Bifunctional Chelator for Actinium-225
35622680	Benzene	oxidative stress	2022	Biomonitoring of Exposure to Urban Pollutants and Oxidativ
35526779	Benzene	hepatotoxicity	2022	Comparison of toxicological effects and exposure levels bet
35462166	Benzene	oxidative stress	2022	Structure-activity relationships of 1,4-bisarylsulfonamido-bo
35445828	Benzene	oxidative stress	2022	Reversal of genetic brain iron accumulation by N,N-bis2-me
35442037	Benzene	hepatotoxicity	2022	Metabolic Activation and Cytotoxicity of Propafenone Medi
35390317	Benzene	increased proliferation	2022	Lymphocyte-Specific Protein-1 Suppresses Xenobiotic-Indu
35366954	Benzene	oxidative stress	2022	Identification of potential pathways and microRNA-mRNA n
35301792	Benzene	oxidative stress	2022	Hsp70 overexpression in Drosophila hemocytes attenuates
35256948	Benzene	oxidative stress	2022	Understanding the physiological functions of the host xeno
35240537	Benzene	oxidative stress	2022	Mulberrin confers protection against hepatic fibrosis by Trin
35204678	Benzene	oxidative stress	2022	Benzaldehyde Attenuates the Fifth Stage Larval Excretory-S
35187629	Benzene	oxidative stress	2022	Evaluating the relationship between the respiratory exposu

PMID 35622680 links 'benzene' to 'oxidative stress'.
Please click on the **PMID** to be forwarded to the associated PubMed
page.

stressor-event : output files

AOPhF_1s1s — Modifié

125 %

Présentation

Zoom

Insérer une catégorie

Insérer

Tableau

Graphique

Texte

Figure

Données multimédias

Comm

Acetaminophen

Acetone

Acrylonitrile

Benzene

Carbon-tetrachloride

Chloroform

PMID 35763560 links 'Acetaminophen' to 'hepatotoxicity'.
Please click on the **PMID** to be forwarded to the associated PubMed page.

also exists in .ods and .csv
versions (no hyperlink for .csv)

AOPPhF_1s1s.xlsx : all stressor-event links; 1 sheet = 1 stressor

Please click on the other
sheets to access data on
other stressors.

stressor-event : output files

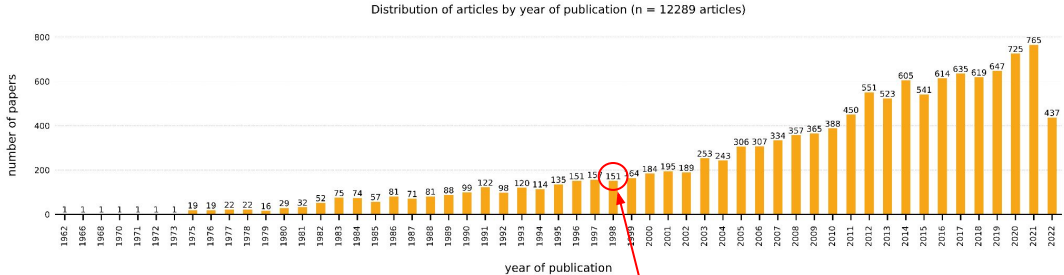
stressor \ event	cyp2e1 activation	hepatotoxicity	increased proliferation	liver cancer	oxidative stress	Total
Acetaminophen	80	2643	22	26	923	3694
Acetone	33	90	34	23	242	422
Acrylonitrile	5	11	2	1	52	71
Benzene	26	62	34	28	486	636
Carbon-tetrachloride	50	1457	79	94	1056	2736
Chloroform	8	210	13	34	171	436
Ethanol	217	939	304	344	4046	5850
Furan	1	69	10	8	53	141
Pyrazole	29	37	19	12	98	195
Vinyl-chloride	5	21	2	72	28	128
Total	454	5539	519	642	7155	14309
Confidence score:						
Low						
Quite Low						
Moderate						
High						
Very High						

Among your output dataset, there are **14309** stressor-event links and **2643** connect 'Acetaminophen' to 'hepatotoxicity'.
The associated confidence score is : **Very High**

also exists in .ods and .csv
versions (no colors for .csv)

stressor-event_links.xlsx : distribution of stressor-event links

stressor-event : output figures (1)

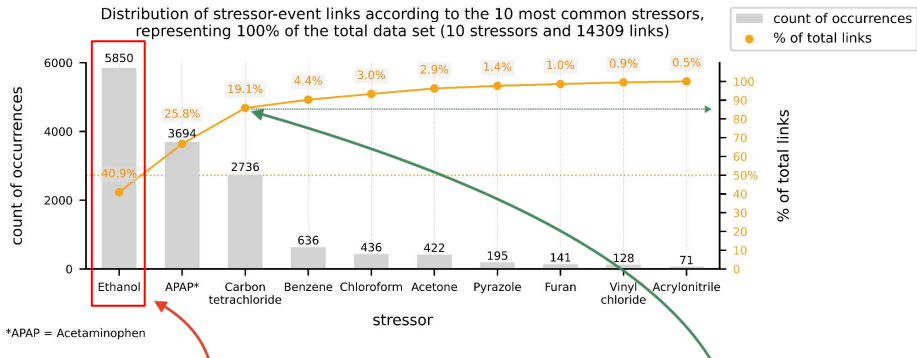


Among your output dataset (n = 12 289 papers), **151** articles were published in 1998.

`distribution_years.pdf` : distribution of articles according to their publication date

This figure is available for both stressor-event and event-event search.

stressor-event : output figures (2)



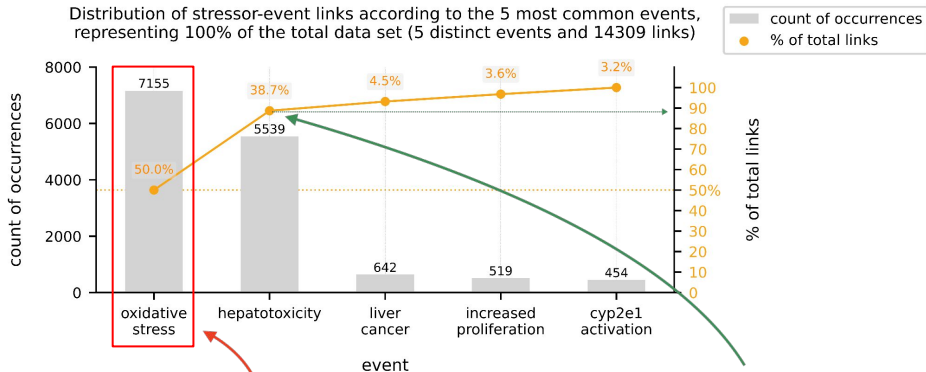
Among your output dataset, there are **14309** stressor-event links and **5850** are related to **'Ethanol'**, which is **40.9%** of the data.

'Ethanol', 'APAP' and 'Carbon-tetrachloride' account for **85.8%** of the data (40.9% + 25.8% + 19.1%).
'Carbon-tetrachloride' alone accounts for **19.1%** of the data.

[distribution_stressors.pdf](#) : distribution of links according to stressors

If there are more than 30 stressors in your output dataset, then the figure displays only the first 30.

stressor-event : output figures (3)



Among your output dataset, there are **14309** stressor-event links and **7155** are related to '**oxidative stress**', which is **50.0%** of the data.

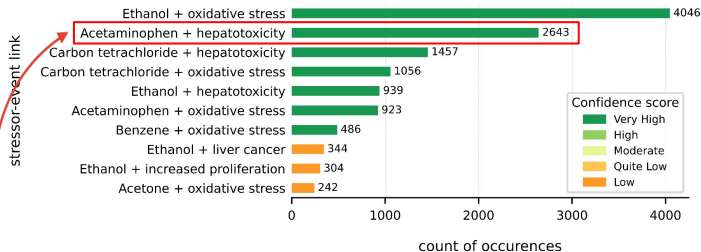
'**Oxidative stress**' and '**hepatotoxicity**' account for **88.7%** of the data (50.0% + 38.7%).
'**hepatotoxicity**' alone accounts for **38.7%** of the data.

[distribution_events.pdf](#) : distribution of links according to events

If there are more than 30 events in your output dataset, then the figure displays only the first 30.

stressor-event : output figures (4)

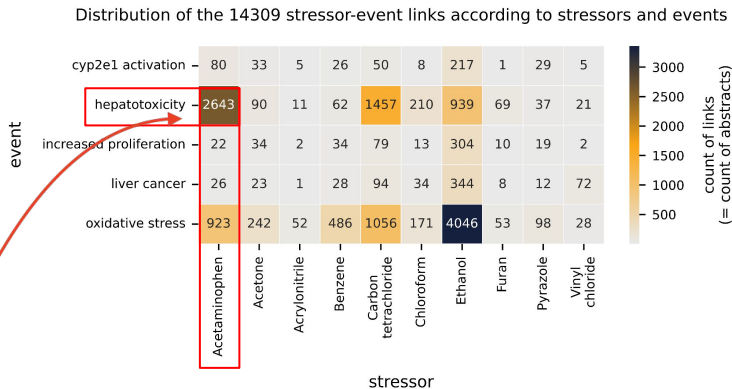
Distribution of stressor-event links according to the 10 most common links, representing 86.9% of the total data set (50 different links and 14309 total links)



Among your output dataset, there are **14309** stressor-event links and **2643** connect 'Acetaminophen' to 'hepatotoxicity'. The associated confidence score is : **Very High**

If there are more than 30 links in your output dataset, then the figure displays only the first 30. Here, we have set the threshold to 10 for convenience.

stressor-event : output figures (5)

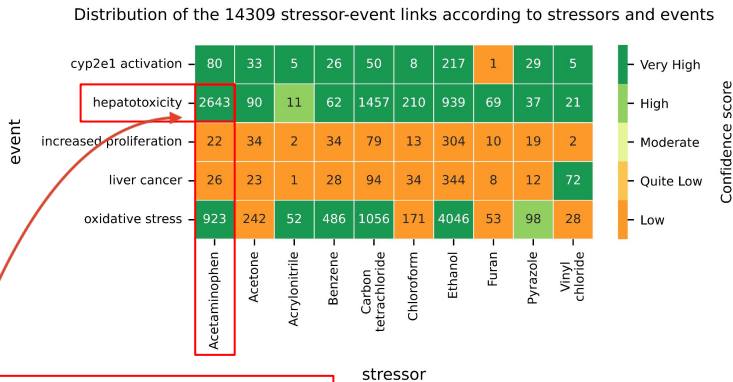


Among your output dataset, there are **14309** stressor-event links and **2643** connect 'Acetaminophen' to 'hepatotoxicity'.

heatmap.pdf : distribution of links according to stressors and events

The color gradient depends on the number of articles.

stressor-event : output figures (6)



Among your output dataset, there are **14309** stressor-event links and **2643** connect 'Acetaminophen' to 'hepatotoxicity'.
The associated confidence score is : **Very High**

heatmap_cs.pdf : distribution of links according to stressors and events

The color gradient depends on the confidence score.

stressor-event : raw results

Folders and files containing the raw result files used for the different figures and outputs :

- raw_AOPhelpFinder
- resume
- raw_scoring

stressor-event : raw_AOPhelpFinder folder



raw_AOP-helpFinder → Contains one .tsv file per stressor.

- Each .tsv file lists all the links (abstracts) extracted by AOP-helpFinder linking the stressor and the events of interest
- Example for Ethanol and different events below

Ethanol

date	title	pmid	event
2022	Protective effects of three flavonoids from <i>Dendrobium huoshanense</i> flowers on alcohol-induced hepatocyte injury via	35774029	oxidative stress
2022	3,4-Dihydroxyphenylethanol and 3,4-dihydroxyphenylacetic acid affect the aggregation process of E46K variant of -syn	35762714	oxidative stress
2022	Alcoholic liver disease: a new insight into the pathogenesis of liver disease.	35761115	hepatotoxicity
2022	Cardioprotection by <i>Citrus grandis</i> L. Peel Ethanolic Extract in Alloxan-Induced Cardiotoxicity in Diabetic Rats.	35757467	oxidative stress
2022	<i>Bruguiera gymnorrhiza</i> L. Lam. Fruit Accelerates Healing in Gastric Injury via the Regulation of the NF- κ B Pathway.	35754686	oxidative stress
2022	Transcriptomics and Network Pharmacology Reveal the Protective Effect of Chaikin Chengqi Decoction on Obesity-Related	35754467	oxidative stress
2022	Resveratrol inhibits the inflammatory response and oxidative stress induced by uterine ischemia reperfusion injury by	35749345	oxidative stress
2022	The Use of Chitosan-Coated Nanovesicles in Repairing Alcohol-Induced Damage of Liver Cells in Mice.	35744025	oxidative stress
2022	Orally administered zingerone does not mitigate alcohol-induced hepatic oxidative stress in growing Sprague Dawley	35734876	oxidative stress
2022	Protective effect of active components of <i>Eucommia ulmoides</i> leaves on gastric ulcers in rats Involvement of the PI3K	35733355	oxidative stress
2022	<i>Alpinia katsumadai</i> Hayata induces growth inhibition and autophagy-related apoptosis by regulating the AMPK and Akt	35730618	liver cancer
2022	<i>Polygonum multiflorum</i> Thunb. Induces hepatotoxicity in SD rats and hepatocyte spheroids by Disrupting the metabolic	35728710	hepatotoxicity
2022	Polydatin attenuates chronic alcohol consumption-induced cardiomyopathy through a SIRT6-dependent mechanism.	35726783	oxidative stress
2022	Loss of SQSTM1/p62 Induces Obesity and Exacerbates Alcohol-Induced Liver Injury in Aged Mice.	35723871	oxidative stress
2022	E Se tea alleviates acetaminophen-induced liver injury by activating the Nrf2 signaling pathway.	35723070	oxidative stress
2022	Mice lacking 4 nicotinic acetylcholine receptors are protected against alcohol-associated liver injury.	35723023	oxidative stress
2022	Loco-regional treatment of hepatocellular carcinoma Role of contrast-enhanced ultrasonography.	35721286	liver cancer

PMID 35774029 links 'Ethanol' to 'oxidative stress'.

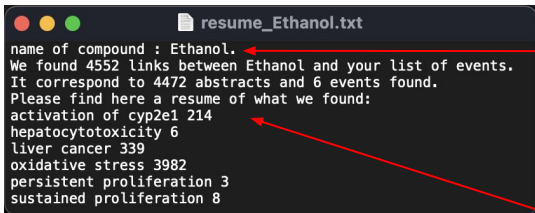
stressor.tsv : stressor-event links

stressor-event : resume folder

resume → Contains one .txt file per stressor.

→ Each .txt file lists information about AOP-helpFinder's stressor-event research

→ Example for Ethanol and different events below



```
resume_Ethanol.txt
name of compound : Ethanol.
We found 4552 links between Ethanol and your list of events.
It correspond to 4472 abstracts and 6 events found.
Please find here a resume of what we found:
activation of cyp2e1 214
hepatocytotoxicity 6
liver cancer 339
oxidative stress 3982
persistent proliferation 3
sustained proliferation 8
```

Information about Ethanol-event research

The file list all the Ethanol-event links extracted by AOP-helpFinder
(e.g. 214 links are found between Ethanol and 'activation of cyp2E1')

All files are contained in the
"resume" folder.

resume.txt : information on stressor-event links

stressor-event : raw_scoring folder

raw_scoring → Contains information about the Confidence scores for each pair of stressor-event links ([more details about the Confidence score in the article](#))

→ Example below

Stressor	Event	Link	Pvalue	pvar	Confidence
Acetaminophen	activation of cyp2e1	78	1.953e-248	9.993e-01	Moderate
Acetaminophen	hepatocytotoxicity	4	2.092e-07	9.543e-01	Moderate
Acetaminophen	liver cancer	26	1.000e+00	NA	Low
Acetaminophen	oxidative stress	898	3.860e-308	7.327e-03	Very High
Acetaminophen	sustained proliferation	2	2.541e-02	1.911e-01	Moderate
Acetone	activation of cyp2e1	33	6.984e-103	9.992e-01	Moderate
Acetone	hepatocytotoxicity	2	1.544e-03	5.313e-02	High
Acetone	liver cancer	23	1.000e+00	NA	Low
Acetone	oxidative stress	237	2.450e-01	NA	Low
Acrylonitrile	activation of cyp2e1	5	6.741e-21	9.999e-01	Moderate
Acrylonitrile	liver cancer	1	1.000e+00	NA	Low
Acrylonitrile	oxidative stress	52	4.339e-06	1.664e-02	High

78 links (abstracts) associating 'acetaminophen' and 'activation of cyp2e1' were extracted by AOP-helpFinder.

→ The Confidence score associated with this link is considered Moderate (details of the Confidence Score calculation in the article)



$$\frac{Cs}{Low} =$$

- Does not mean that a link does not exist.
- Warn you manually check the result by reading the articles provided.

event-event search

event-event : output files (1)

PMID	event1	event2	date	title
35775504	oxidative stress	hepatotoxicity	2022	Evaluation of hepatotoxicity and nephrotoxicity induced by
35771985	oxidative stress	hepatotoxicity	2022	Protection Against Drug-Induced Liver Injuries Through Nut
35765203	oxidative stress	hepatotoxicity	2022	The potential curative role of Avena sativa extract against o
35760093	oxidative stress	liver cancer	2022	The role of protein kinases as key drivers of metabolic dysfu
35739991	oxidative stress	hepatotoxicity	2022	Effect of Theobroma cacao L. on the Efficacy and Toxicity of
35739723	oxidative stress	hepatotoxicity	2022	Mechanism-driven modeling of chemical hepatotoxicity usi
35737028	oxidative stress	hepatotoxicity	2022	Role of Nrf2 Nucleus Translocation in Beauvericin-Induced C
35730503	oxidative stress	increased proliferatio	2022	MiR-106a facilitates the sensorineural hearing loss induced
35725022	oxidative stress	increased proliferatio	2022	Quercetin in Tonglong Qibi decoction ameliorates testoster
35716303	oxidative stress	hepatotoxicity	2022	Silver nanoparticles induced hepatotoxicity via the apoptotic
35715032	oxidative stress	hepatotoxicity	2022	Toxicological assessment of sublethal dose of acetamiprid i
35671811	oxidative stress	hepatotoxicity	2022	Vildagliptin alleviates liver fibrosis in NASH diabetic rats via
35658244	oxidative stress	hepatotoxicity	2022	Hispanic ethnicity and the rs4880 variant in SOD2 are assoc

PMID 35775504 links 'oxidative stress' to 'hepatotoxicity'.
Please click on the **PMID** to be forwarded to the associated PubMed
page.

event-event : output files (2)



event1 \ event2	cyp2e1 activation	hepatotoxicity	increased proliferation	liver cancer	oxidative stress
cyp2e1 activation		x	x	x	x
hepatotoxicity	21		x	x	x
increased proliferation	0	3		x	x
liver cancer	1	28	29		x
oxidative stress	46	753	178	76	
Confidence score:					
Low					
Quite Low					
Moderate					
High					
Very High					

Among your output dataset, **46** event-event links connect 'cyp2e1 activation' to 'oxidative stress'.

The associated confidence score is : **Very High**

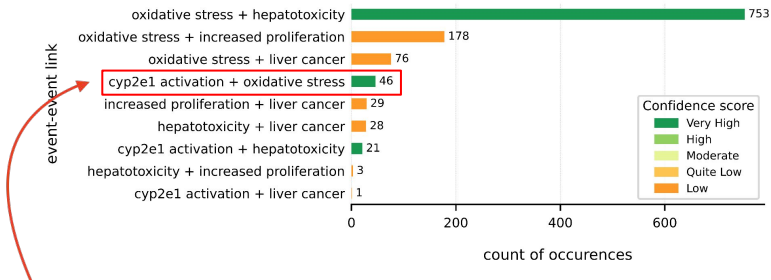
also exists in .ods and .csv
versions (no colors for .csv)

event_event_links.xlsx : distribution of event-event links

 The table is symmetrical, so the upper triangular part does not contain any values to avoid data redundancy. 

event-event : output figures (1)

Distribution of event-event links according to the 9 most common links, representing 100% of the total data set (9 different links and 1135 total links)



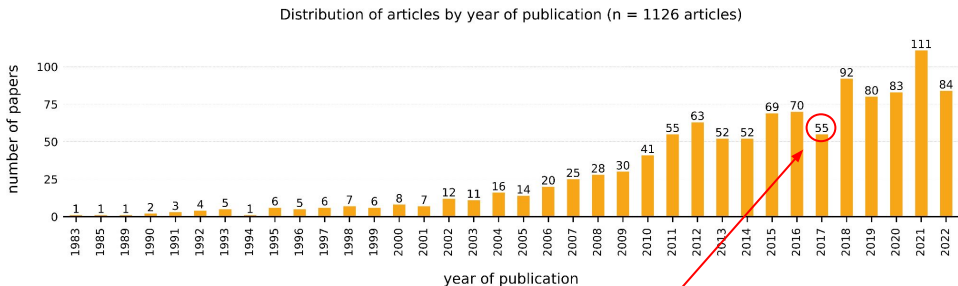
Among your output dataset, there are **1135** event-event links and **46** connect 'cyp2e1 activation' to 'oxidative stress'.

The associated confidence score is : **Very High**

distribution_scores.pdf : distribution of links according to the confidence score and number of links

If there are more than 30 links in your output dataset, then the figure displays only the first 30.

event-event : output figures (2)



Among your output dataset (n = 1126 papers), 55 articles were published in 2017.

[distribution_years.pdf](#) : distribution of articles according to their publication date

This figure is available for both stressor-event and event-event search.

event-event : raw results

Folders and files containing the raw results files used for the different figures and outputs :

- raw_AOPhelpFinder
- raw_scoring

event-event : raw_AOPhelpFinder folder

raw_AOP-helpFinder → Contains one .tsv file

→ Lists all the links (abstracts) extracted by AOP-helpFinder connecting events of interest

→ Example below

date	title	pmid	event1	event2
2022	Evaluation of hepatotoxicity and nephrotoxicity induced by Fenpyr	35775504	oxidative stress	hepatotoxicity
2022	Protection Against Drug-Induced Liver Injuries Through Nutraceutic	35771985	oxidative stress	hepatotoxicity
2022	The potential curative role of Avena sativa extract against oxidative	35765203	oxidative stress	hepatotoxicity
2022	The role of protein kinases as key drivers of metabolic dysfunction-	35760093	oxidative stress	liver cancer
2022	Effect of Theobroma cacao L. on the Efficacy and Toxicity of Doxor	35739991	oxidative stress	hepatotoxicity
2022	Mechanism-driven modeling of chemical hepatotoxicity using struc	35739723	oxidative stress	hepatotoxicity
2022	Role of Nrf2 Nucleus Translocation in Beauvericin-Induced Cell Dar	35737028	oxidative stress	hepatotoxicity
2022	MIR-106a facilitates the sensorineural hearing loss induced by oxid	35730503	oxidative stress	increased proliferation
2022	Quercetin in Tonglong Qibi decoction ameliorates testosterone-indu	35725022	oxidative stress	increased proliferation
2022	Silver nanoparticles induced hepatotoxicity via the apoptotic/antiapo	35716303	oxidative stress	hepatotoxicity

PMID 35775504 links 'oxidative stress' to 'hepatotoxicity'.

output-eventevent.tsv : stressor-event links

event-event : raw_scoring folder

raw_scoring → Contains information about the Confidence scores for each pair of event-event links ([more details about the Confidence score in the article](#))

→ Example below

Event 1	Event 2	Link	Pvalue	pvar	Confidence
cyp2e1 activation	oxidative stress	46	1.452e-18	6.219e-18	Very High
cyp2e1 activation	liver cancer	1	9.999e-01	NA	Low
cyp2e1 activation	hepatotoxicity	21	1.158e-23	3.271e-22	Very High
oxidative stress	hepatotoxicity	753	6.212e-202	1.752e-201	Very High

46 links (abstracts) associating 'cyp2e1 activation' and 'oxidative stress' were extracted by AOP-helpFinder.

→ The Confidence score associated with this link is considered Very High (details of the Confidence Score calculation in the article)



$\frac{Cs}{Low} =$

- Does not mean that a link does not exist.
- Warn you manually check the result by reading the articles provided.