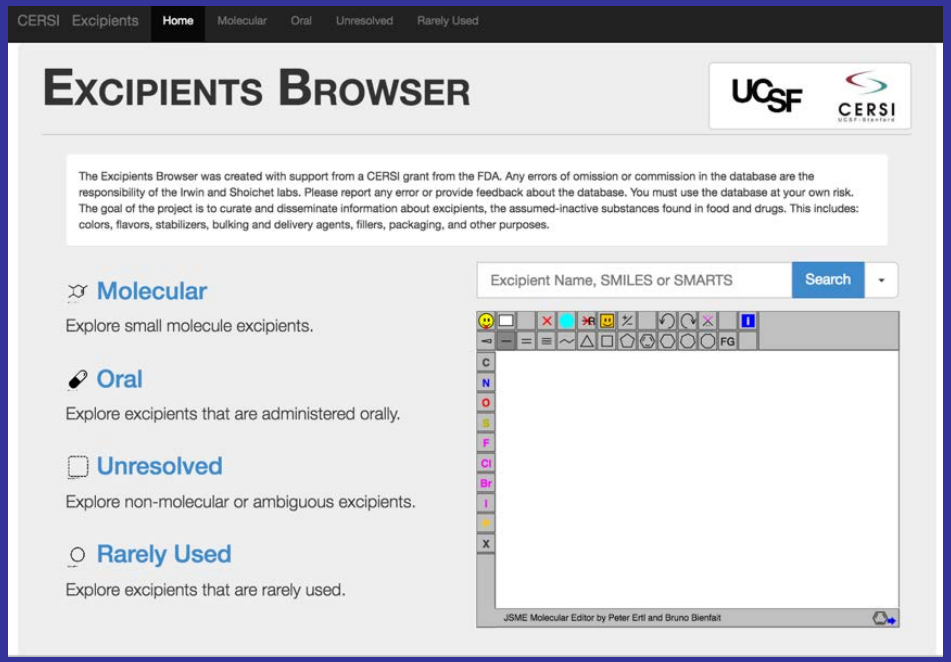
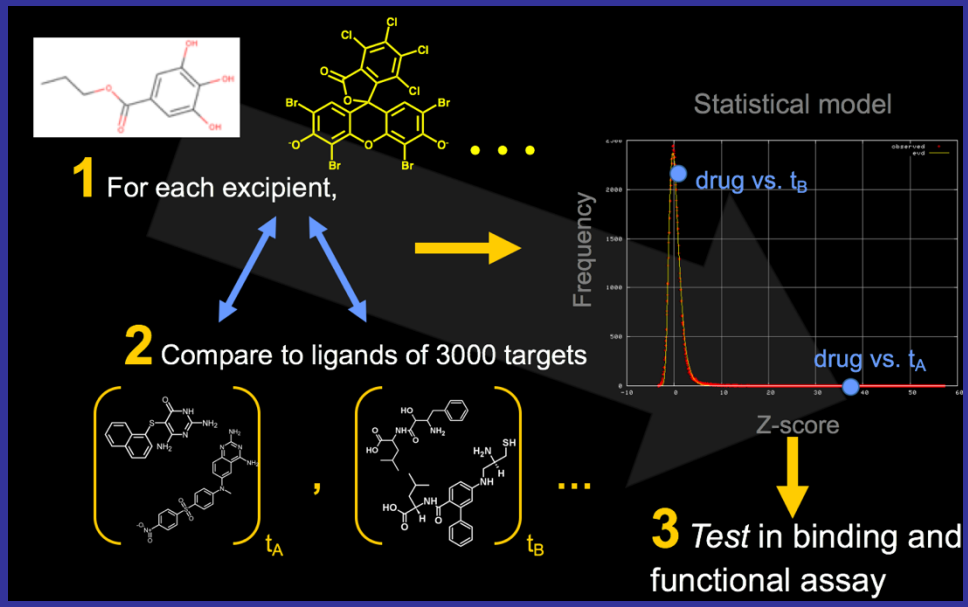
Open access excipients, exploring their activities

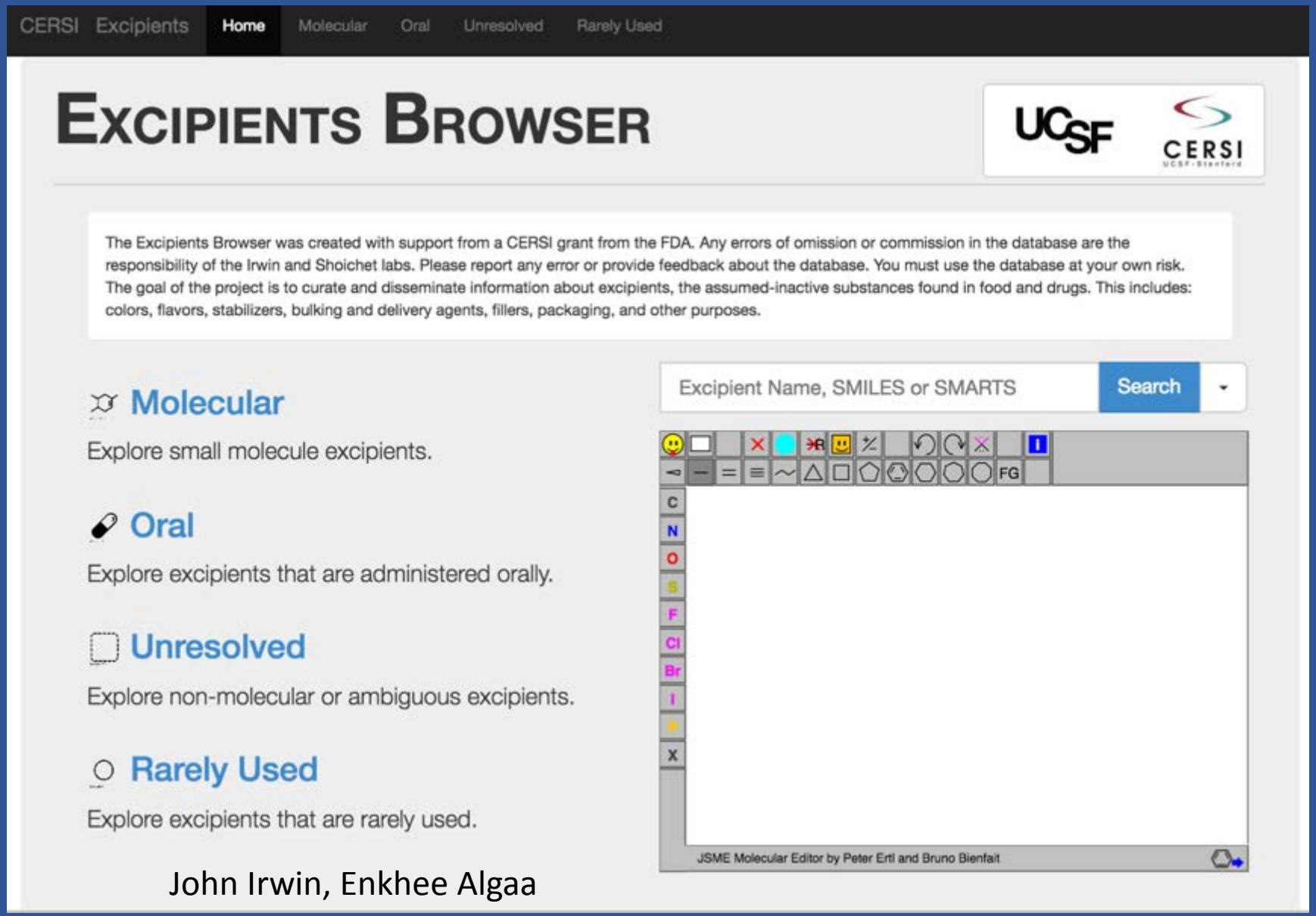




A tool to interrogate excipient properties, where they can be sourced, their use with drugs

Do these “inactive” ingredients have specific molecular targets

A public access excipients browser http://excipients.ucsf.bkslab.org/



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Properties, drugs, trial formulations, vendors for ~550 molecular excipients

CERSI Excipients Home Molecular Oral Unresolved Rarely Used

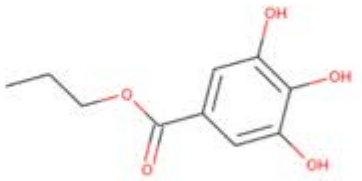
PROPYL GALLATE

Molecular Excipient

SMILES CCCOC(=O)c1cc(O)c(O)c(O)c1

Mwt.	LogP	HBD	HBA	PSA	RB	CSP3
212.0	1.4	3	5	87.0	3	0.3

UNII 8D4SNN7V92
CAS 121799
ZINC ID(s) ZINC1532172
Availability Present in 57 ZINC catalogs



Known Active Genes

There has not been any activity reported at 10μM or less for this excipient (per ChEBML)

Clinical Trials

This compound has been an intervention in the following clincial trials (per clinicaltrials.gov).

Code	Date	Title	Phase	Status
NCT02205320	2014-02-01	A Comparative, Crossover, Pharmacokinetic, Pharmacodynamic and Safety Study of Three Forms of PEG-G-CSF in Normal Healthy Volunteers	Phase 1	Recruiting
NCT01980940	2013-12-01	The Single Dose Pharmacokinetics of Two and Proof of Efficacy of One New Etoricoxib Gel Formulation in Participants With Osteoarthritis (MK-0663-168)	Phase 1/Phase 2	Completed
NCT01450098	2011-10-01	A Study of LY2484595 in Healthy Subjects	Phase 1	Completed
NCT00369928	2006-08-01	Evaluation of 2 Oral Doses of PG-760564 in Rheumatoid Arthritis (RA) Patients Receiving Methotrexate	Phase 2	Completed
NCT00801814	2006-04-01	Effect of Escalating Doses of a Novel Viscous Polysaccharide on Postprandial Glycemia	Phase 2/Phase 3	Completed

Dosages

Route	Formulation	Potency
Intramuscular	Injection	
Oral	Capsule	0.16MG
Oral	Capsule, Soft Gelatin	2MG
Oral	Concentrate	0.02%
Oral	Suspension	
Oral	Tablet	1.36MG
Oral	Tablet, Extended Release	0.07MG
Oral	Tablet, Film Coated	0.04MG
Oral	Tablet, Sustained Action	0.06MG
Oral	Tablet, Sustained Action, Coated	0.04MG
Topical	Emulsion, Cream	

Products using propyl gallate…

Purchasable Analogs in ZINC (Browse)

Browse on ZINC

Products Using Propyl Gallate

Brand (Manufacturer)	Generic Name (Route)
Childrens Delsym Cough Plus Cold Night Time (Reckitt Benckiser LLC)	Acetaminophen, Diphenhydramine Hydrochloride, And Phenylephrine Hydrochloride (ORAL)
Mucus Relief Cold And Sinus Maximum Strength (Dolgencorp, Inc. (DOLLAR GENERAL & REXALL))	Acetaminophen, Guaifenesin, Phenylephrine Hcl (ORAL)
Kmart - Fast Maximum Severe Congestion And Cough (Kmart Corporation)	Dextromethorphan Hydrobromide, Guaifenesin And Phenylephrine Hydrochloride (ORAL)
Rouge Dior 850 Red Serum (Parfums Christian Dior)	Octinoxate (TOPICAL)
Advil Congestion Relief (Lil' Drug Store Products, Inc)	Ibuprofen And Phenylephrine Hydrochloride (ORAL)
Mucus Relief Severe Congestion And Cough (MEIJER, INC.)	Dextromethorphan Hbr, Guaifenesin, Phenylephrine Hcl (ORAL)
Childrens Dimetapp Multisymptom Cold And Flu (Richmond Division of Wyeth)	Acetaminophen, Chlorpheniramine Maleate, Dextromethorphan Hbr, Phenylephrine Hcl (ORAL)
Fresh Sugar Passion Tinted Lip Treatment Spf 15 (Fresh, Inc.)	Octinoxate, Avobenzone (TOPICAL)
Tussnex Fm Cold And Sinus (Guardian Drug Company)	Acteaminophen, Guaifenesin, Phenylephrine Hcl (ORAL)

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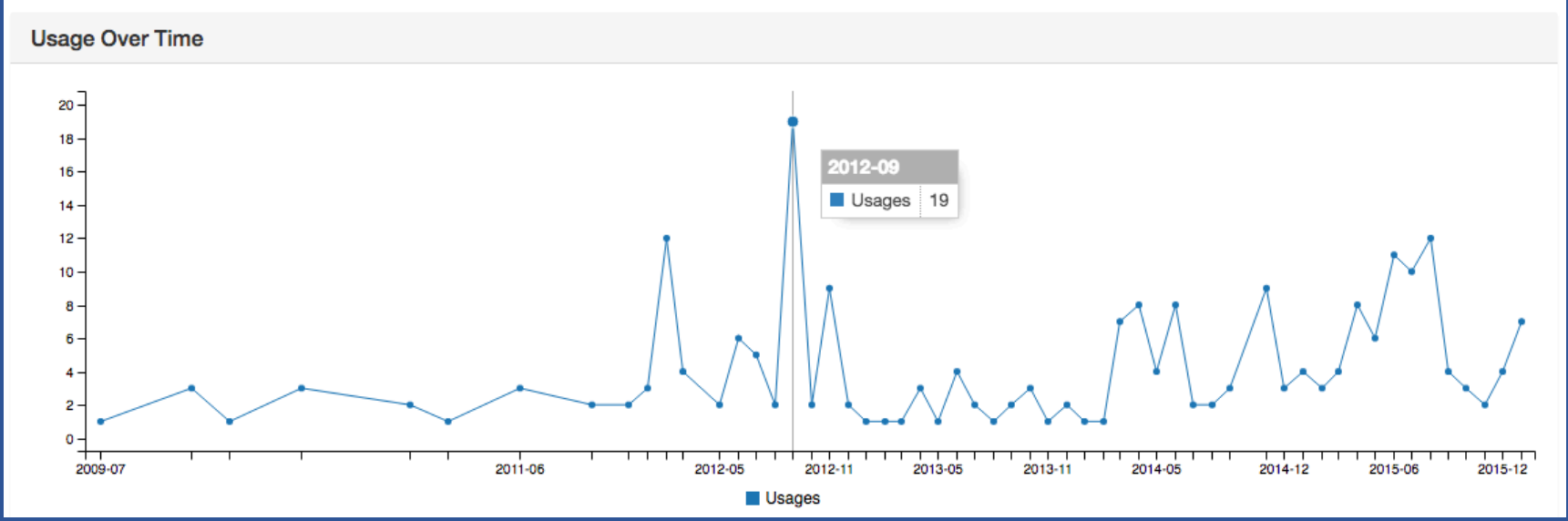
Excipients linked to public information

1. Approved formulations over time (from openFDA)



2. Purchasability (via ZINC)

Vendors (37 Total) — 47 Items Total

ChemBridge	5108506
Alfa-Aesar	A10877
Matrix Scientific	119792
Molport BB	MolPort-001-789-639
Ryan Scientific BB	047-99470
Sigma Aldrich (Building Blocks)	02370|SIGMA, 1576800|USP, 48710|SIAL, P3130|SIGMA, P3640000|SIAL, PHR1118|SIAL, V001246|VETEC, V001693|VETEC, W294705|ALDRICH

3. Link to functional databases (via ZINC)

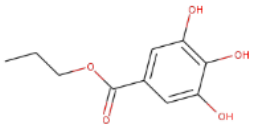
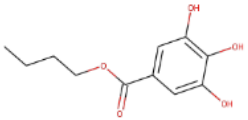
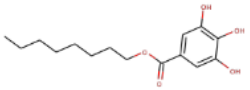
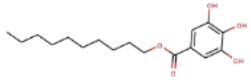
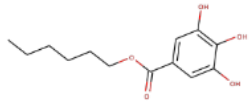
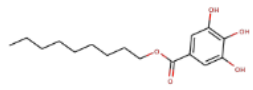
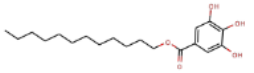
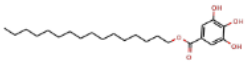
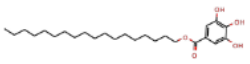
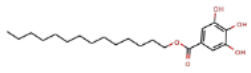
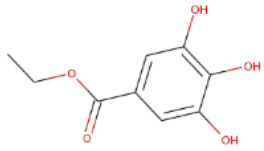
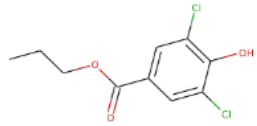
Annotated Catalogs (16 Total) — 17 Items Total

BindingDB.org	50032154
Biocyc via PubChem	CPD-6542
Bitter DB	748
ChEMBL20	CHEMBL7983
ChEMBL 21	CHEMBL7983
ChEMBL 22	CHEMBL7983
ChEMBL DrugStore	CHEMBL7983
Food Database	HMDB33835
HMDB Food	HMDB33835
Human Metabolome Database	HMDB33835

Purchasable analogs for research

Via ZINC

« 1 » Get Total / substances / subsets / for-sale Filters Lookup

ZINC1532172 Pg  1.00	**ZINC1665979** Butyl Gallate  0.80	**ZINC1632635** E311  0.75	**ZINC2002123** Decyl Gallate  0.75	**ZINC2510146** Hexyl Gallate  0.75	**ZINC2565997** Nonyl Gallate  0.75
ZINC33861415 E312  0.75	**ZINC33861467** Hexadecyl Gallate  0.75	**ZINC33861487** Octadecyl Gallate  0.75	**ZINC49878676** Tetradecyl Gallate  0.75	**ZINC21790** Nipa 48  0.72	**ZINC2566191**  0.71

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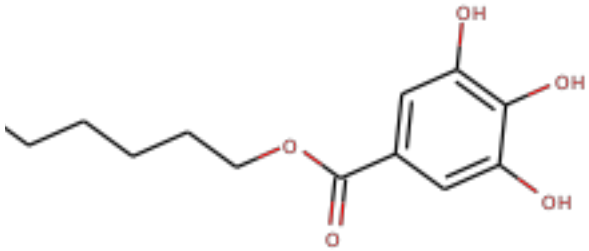
Detailed purchasing links to vendors:

ZINC1632635 (E311)



Vendors (29 Total) — 32 Items Total

Alfa-Aesar	L06081
Combi-Blocks	QA-4025
Matrix Scientific	099019
Molport BB	MolPort-001-789-
Sigma Aldrich (Building Blocks)	06717|SIAL, 289 48700|ALDRICH,

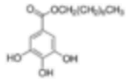
SIGMA-ALDRICH®
A Part of MilliporeSigma

Search term:"06717|SIAL"

1 match found for 06717|SIAL — Sort By Relevance

Octyl gallate

1 Product Result | Match Criteria: Keyword — Properties



Linear Formula: $3,4,5\text{-}(HO)_3C_6H_2CO_2(CH_2)_7CH_3$ | Molecular Weight: 282.33 | CAS Number: 1034-01-1

06717 analytical reference material (Sigma-Aldrich) — SDS | close

SKU-Pack Size	Availability	Price (USD)	Quantity
06717-500MG	Only 2 left in stock (more on the way) - FROM	77.50	0

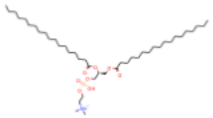
Bulk orders?

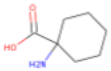
ADD TO CART

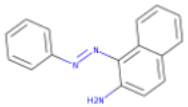
Search by route of administration

« 1 2 ... 69 70 » 2514 Total

Route: Oral Search


1,2-DISTEAROYL-SN-GLYCE...


1-AMINOCYCLOHEXANECA...

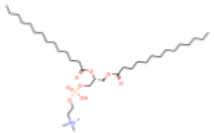

1-(PHENYLAZO)-2-NAPHTHY...

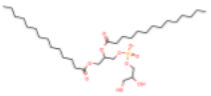
2212 FINE BLACK

Oral

Route: Intravenous Search

I.V.


1,2-DIMYRISTOYL-SN-GLYC...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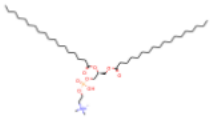
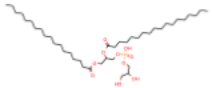
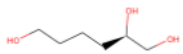
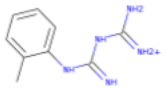

1,2-DISTEAROYL-SN-GLYCE...

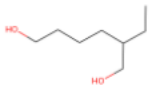

1,2-DISTEAROYL-SN-GLYCE...

« 1 2 ... 16 17 » 602 Total

Route: Topical Search


1,2,6-HEXANETRIOL


1-O-TOLYLBIGUANIDE

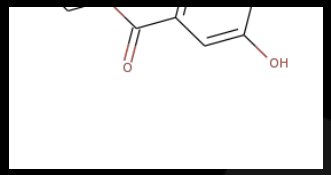

2-ETHYL-1,6-HEXANEDIOL

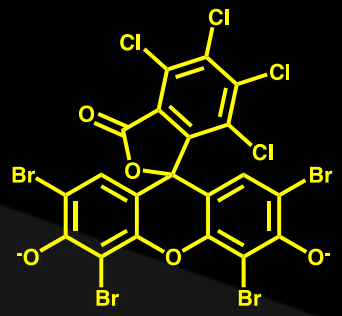

ACETIC ACID

Topical

John Irwin, Enkhee Algaa

Biological targets for inactive ingredients? Predicting 550 excipients vs. 3000 proteins

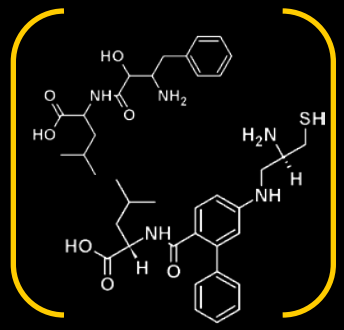




1 For each excipient,

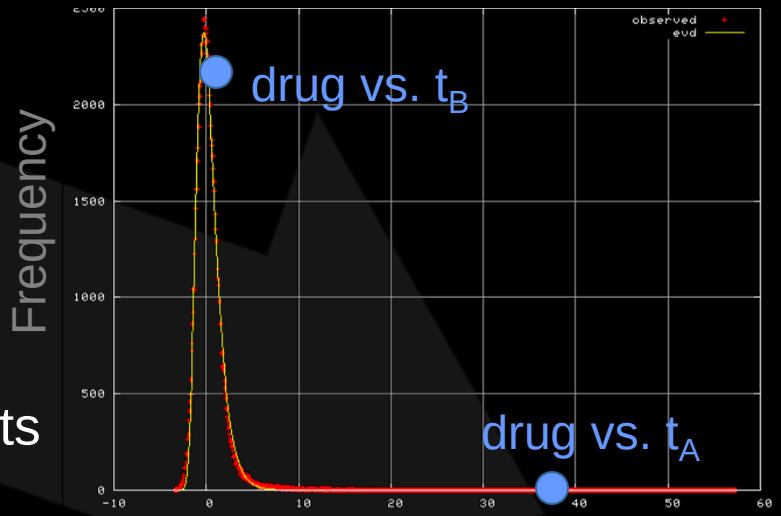
2 Compare to ligands of 3000 targets

,



...

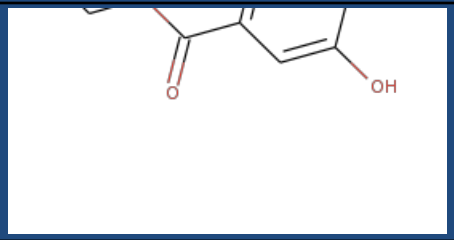
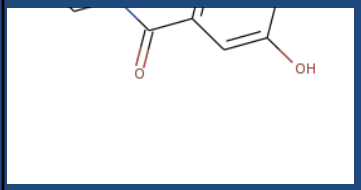
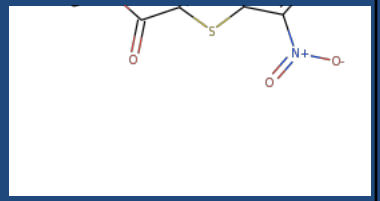
Statistical model

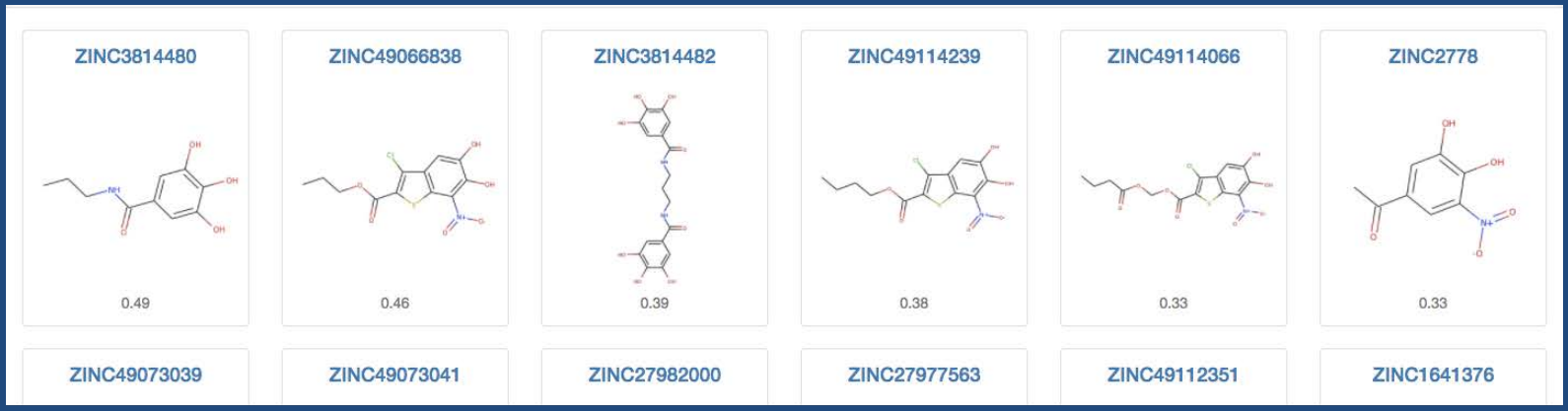


3 *Test* in binding and functional assay

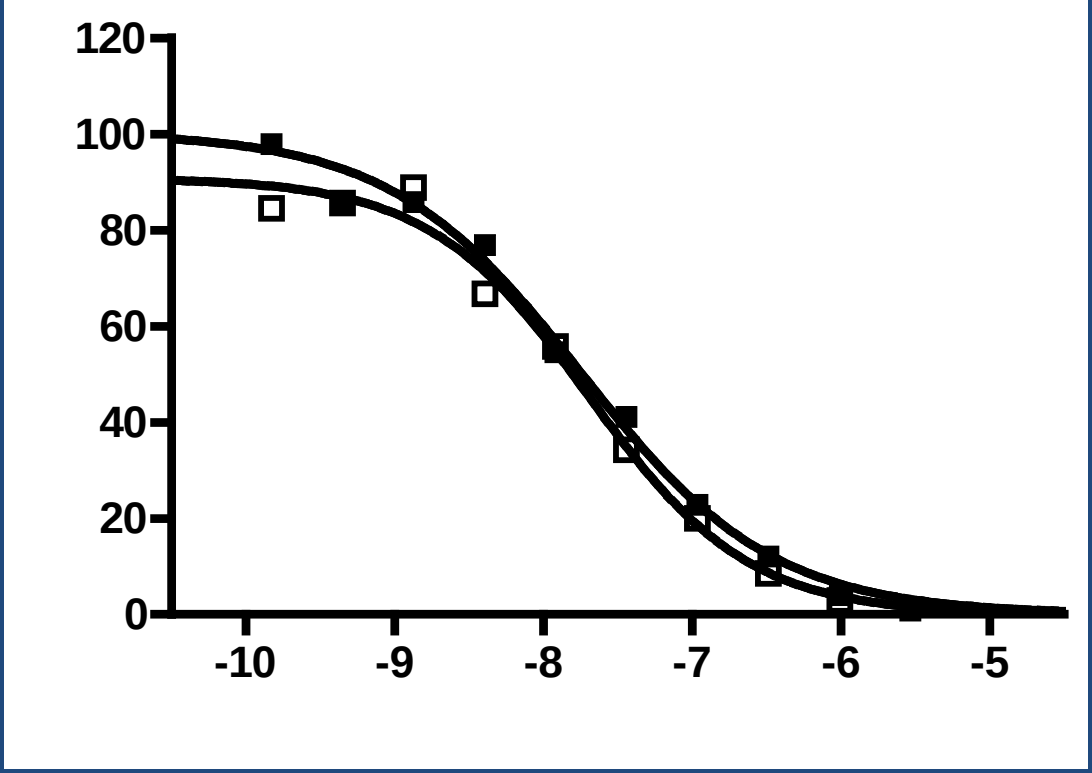
Keiser, ***Nature*** 2009; Lounkine, ***Nature*** 2012

Example: SEA predicts propyl gallate will hit COMT (from its chemical similarity to COMT's ***ligands***)

Propyl Gallate (antioxidant)	
Prediction: Catechol O-Methyltransferase (COMT) **SEA E-value: 2.2 x 10^{-13}**	Known binders (IC_{50} < 10uM):  



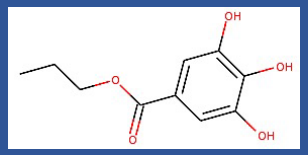
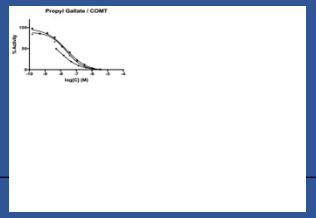
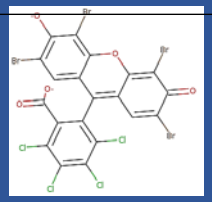
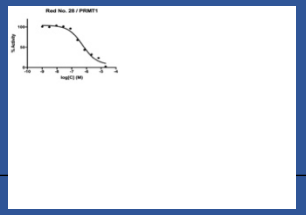
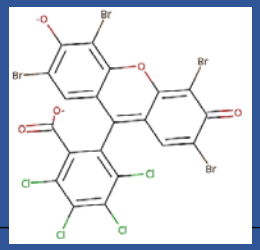
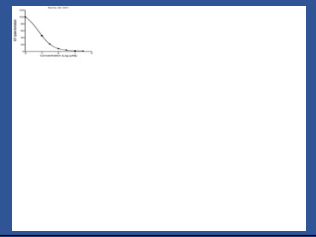
Propyl Gallate inhibits COMT at 20 nM



Josh Pottel

Systematic prediction & testing for excipient targets

Excipients	Predictions	Tested	Confirmed	False Positive - Aggregators
445	21565	73	31	4

Excipient	Structure	Target	SEA Score	IC50	D/R Curve
Propyl Gallate		COMT	7.5×10^{-22}	20 nM	
D&C Red No. 28 (Phloxine B)		PRMT1 (Protein arginine methyl-transferase)	2.6×10^{-19}	700 nM	
D&C Red No. 28 (Phloxine B)		SLC22A6 (OAT1)	7.8×10^{-16}	64 nM	

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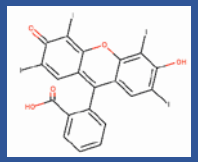
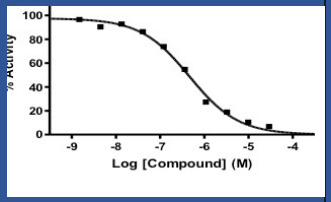
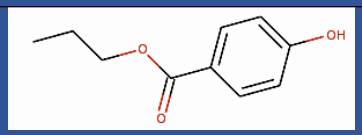
Systematic prediction & testing for excipient targets

Excipient	Structure	Target	SEA Score	IC50	D/R Curve
FD&C Red No. 3		PRMT1	$3.7\ 10^{-17}$	460 nM	
Propyl-paraben		ESR1/ESR2 (Estrogen receptor alpha/beta)	$1.7x\ 10^{-14}$ $2.6x\ 10^{-12}$	66%/ 58% @ 10uM	N/A
Thymol		5-HT2B (Serotonin receptor 2B)	via propofol	9 uM	N/A

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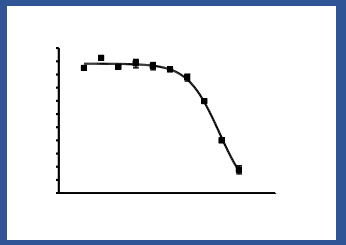
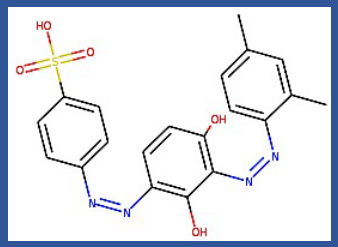
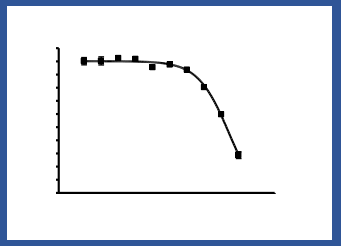
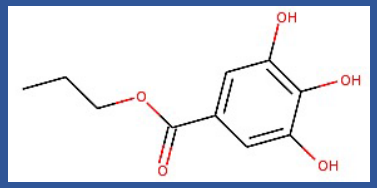
Systematic prediction & testing for excipient targets

Excipient	Structure	Target	SEA Score	IC50	D/R Curve
Acid Orange 20		BRD4	1.4×10^{-25}	25 uM	
D&C Brown No. 1		BRD4	1.1×10^{-27}	46 uM	
Propyl Gallate		Tyrosine hydroxylase	via dopamine targets	<5 uM	100% inhibition @ 30uM

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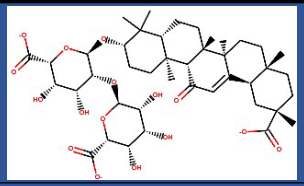
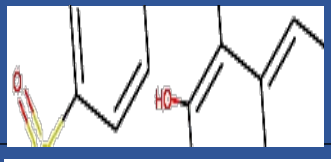
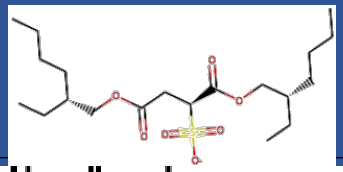
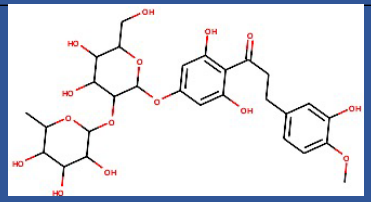
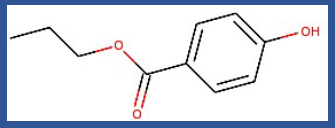
Gut transporters as priority targets (16 hits for 31 predictions tested)

Excipient	Structure	Ki (uM)
Glycyrrhizin		165
D&C Orange No. 4		1.9
Docusate Sodium		2.3
Lauryl Sulfate		2.8
Neohesperidin Dihydrochalone		18
Propylparaben		198

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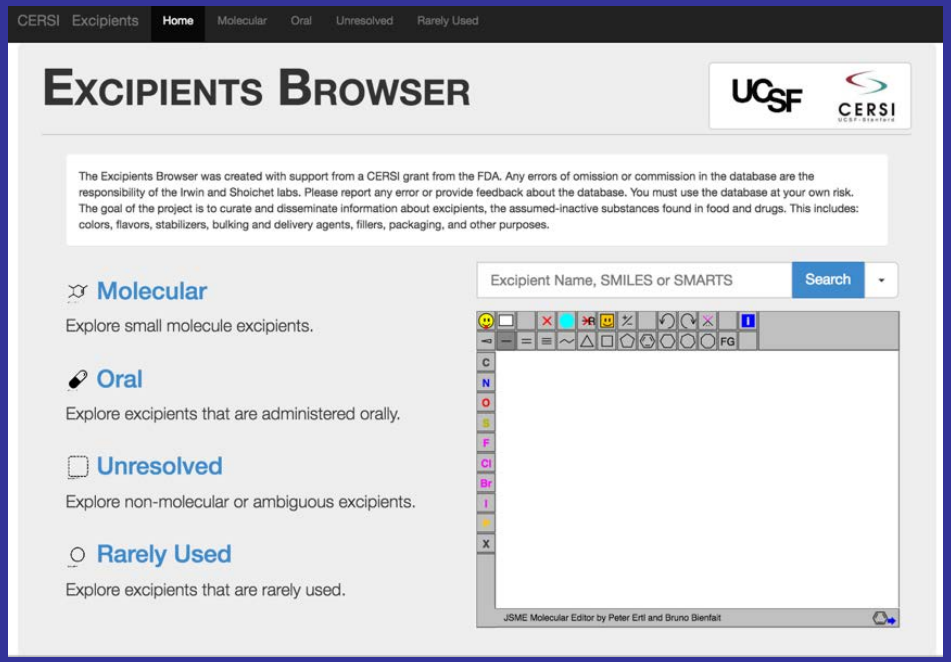
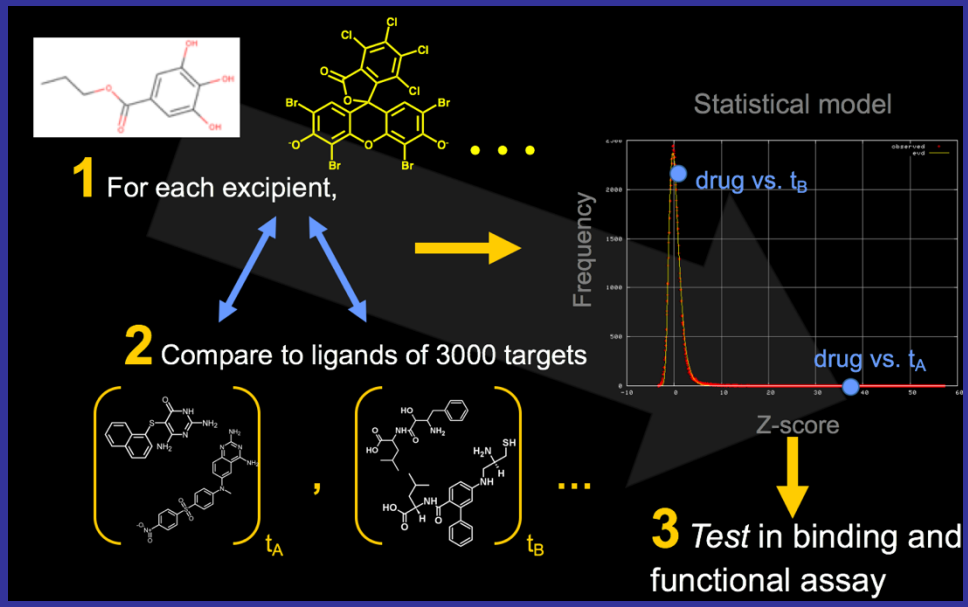
Open access excipients, exploring their activities





A tool to interrogate excipients

These “inactive” ingredients have specific on-target activities