A Comprehensive Computational Pharmacokinetics Identification of Biotransformed Leads from *Curcuma Caesia* Roxb

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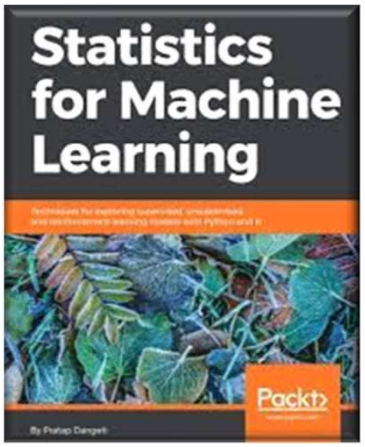
Herbal Medicine

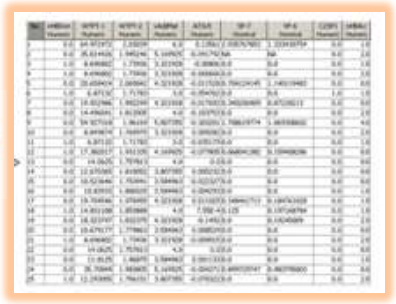
RISE IN GLOBAL HERBAL MARKET

Drug Discovery Paradigm

Duxin S et al 2022

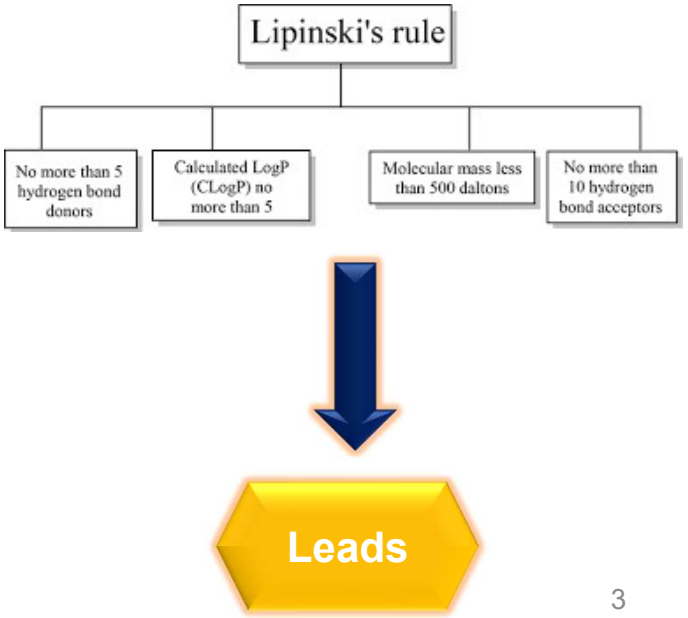
In silico Methods in Drug Discovery





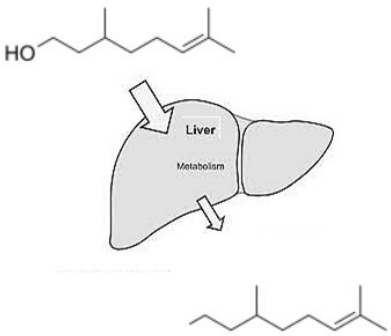
Molecular Descriptors

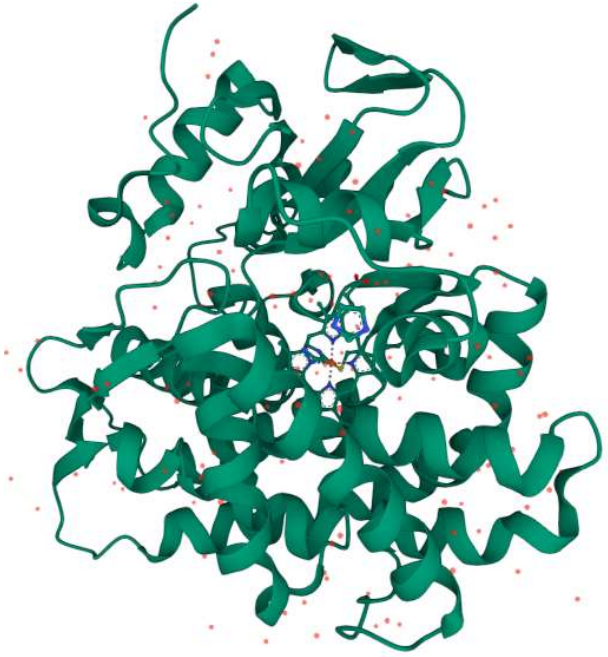
ADMET Druglikeness etc..



David D et al 2019, Lipinski et al., 2001, Lagorce et al., 2012

Metabolism





Cytochrome P450 PDB 4L36

Bio transformed Leads

?

ADMET

(Tarcsay and Keseru, 2011,Schmidt et al., 2014 and Sliwoski et al., 2014)

PLANT CHOSEN FOR THE PRESENT STUDY

Scientific classification

Kingdom: Plantae

Order: Zingiberales

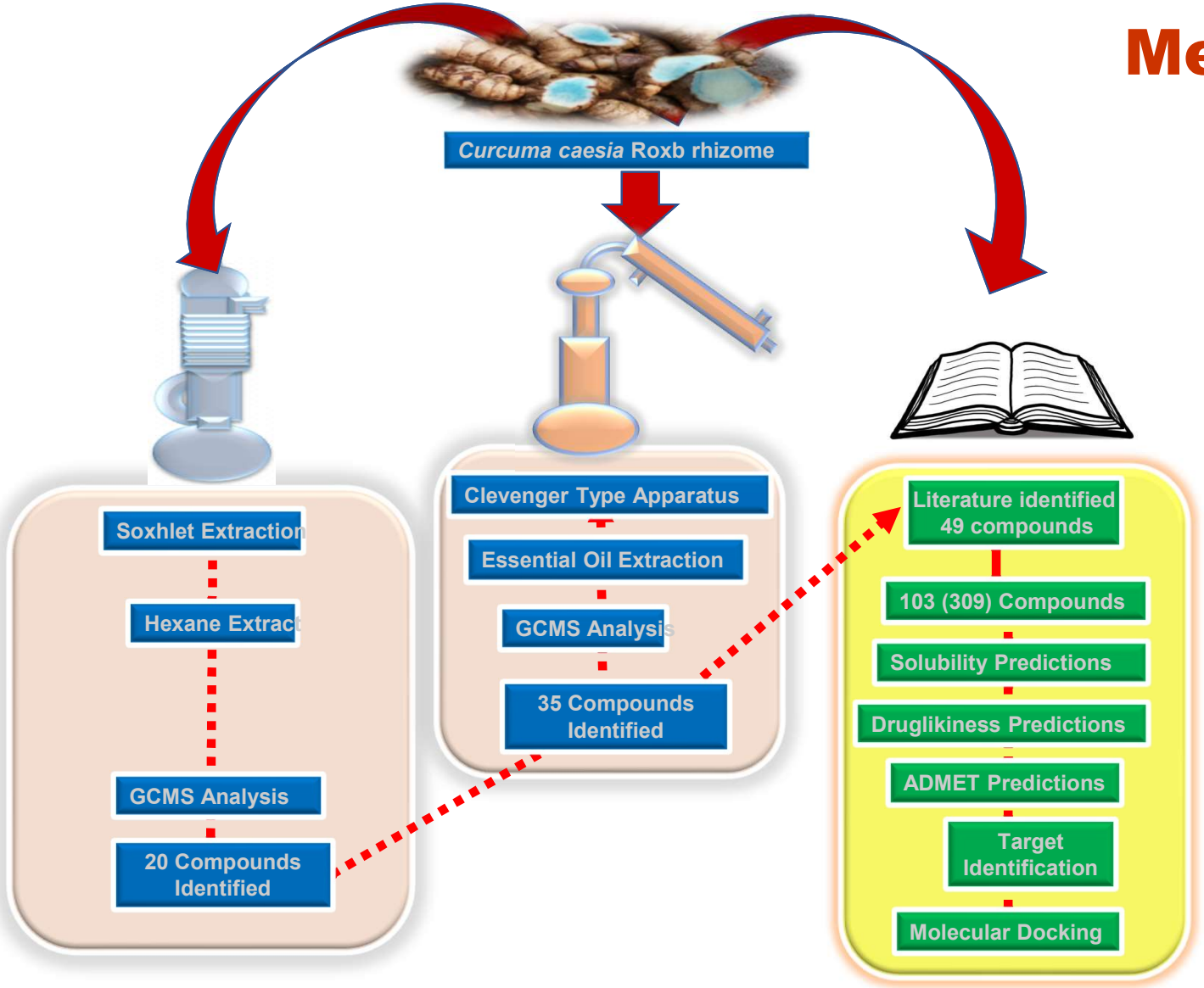
Family: Zingiberaceae

Genus: *Curcuma*

Species: *C. caesia*

Binomial name: *Curcuma caesia* Roxb.

Methodology



Results

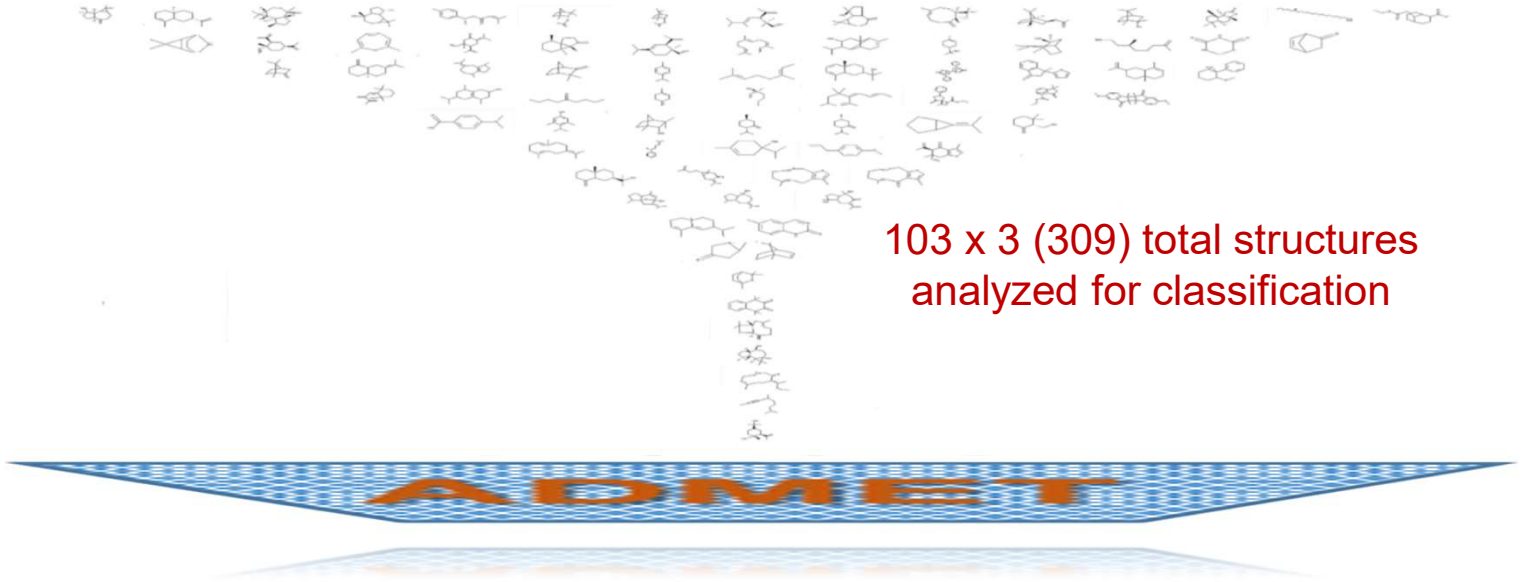
Druglikiness Assessment

- 103 compounds was subjected to ANN based druglikiness assessment which includes Lipinski's rule, CMC-like, MDDRF like and WDI-like rule.
  - Lipinski's rule of five **all qualified**
  - CMC-like rule **70% qualified**
  - **Lead like 34% qualified**
  - MDDR-like predictions (mid-structures)

    94% qualified
  - WDI-like predictions (90% cut off)

    71% qualified

In silico ADMET Screening



103 x 3 (309) total structures analyzed for classification

Lead

Target Selection

Activity prediction and Docking

- PharmMapper target prediction showed common target Retinoic acid receptor human proteins Retinoic acid as a powerful inhibitor of PIN1 isomerase enzyme, central signaling enzyme of oncogenic pathways.

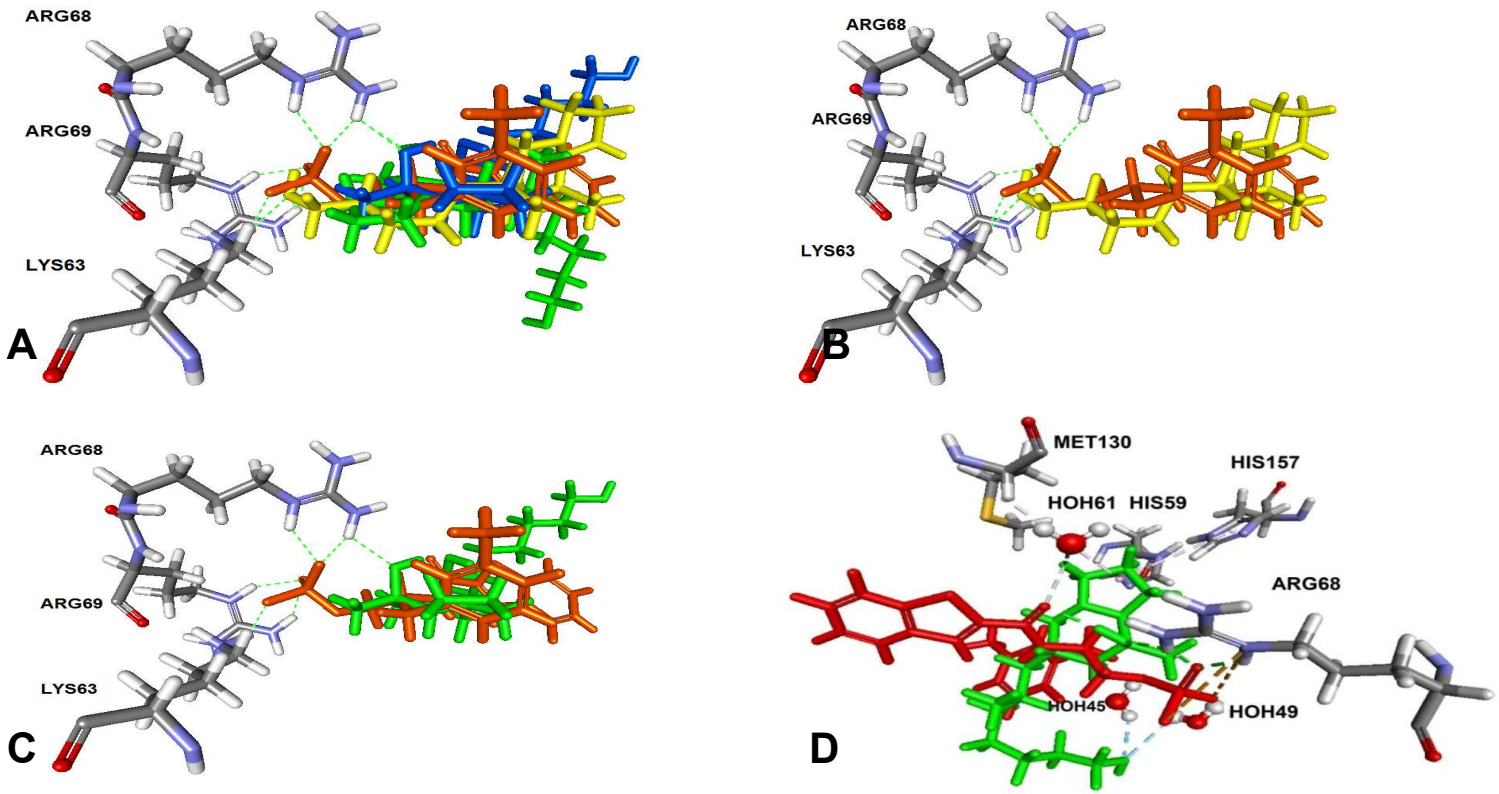
✓ PDB code: 3ikg

Rank	PDB ID	Target Name	Number of Feature	Fit Score	Normalized Fit Score	z'-score
1	2IIT	Dipeptidyl peptidase 4	6	3.791	0.6318	3.56472
2	2QGV	Dipeptidyl peptidase 4	7	3.717	0.531	3.50351
3	1V40	Glutathione-requiring prostaglandin D synthase	8	3.677	0.4596	3.42998
4	1DVU	Transthyretin	5	3.561	0.7122	3.36036
5	1KON	Chloride intracellular channel protein 1	5	3.593	0.7185	3.16909
6	1HS6	Leukotriene A-4 hydrolase	9	3.744	0.4161	3.01153
7	2P1U	Retinoic acid receptor RXR-alpha	9	3.818	0.4242	2.88884
8	1FCX	Retinoic acid receptor gamma	9	3.768	0.4187	2.76885
9	1Q6J	Tyrosine-protein phosphatase non-receptor type 1	8	3.559	0.4449	2.76064
10	1FD0	Retinoic acid receptor gamma	8	3.783	0.4728	2.56212

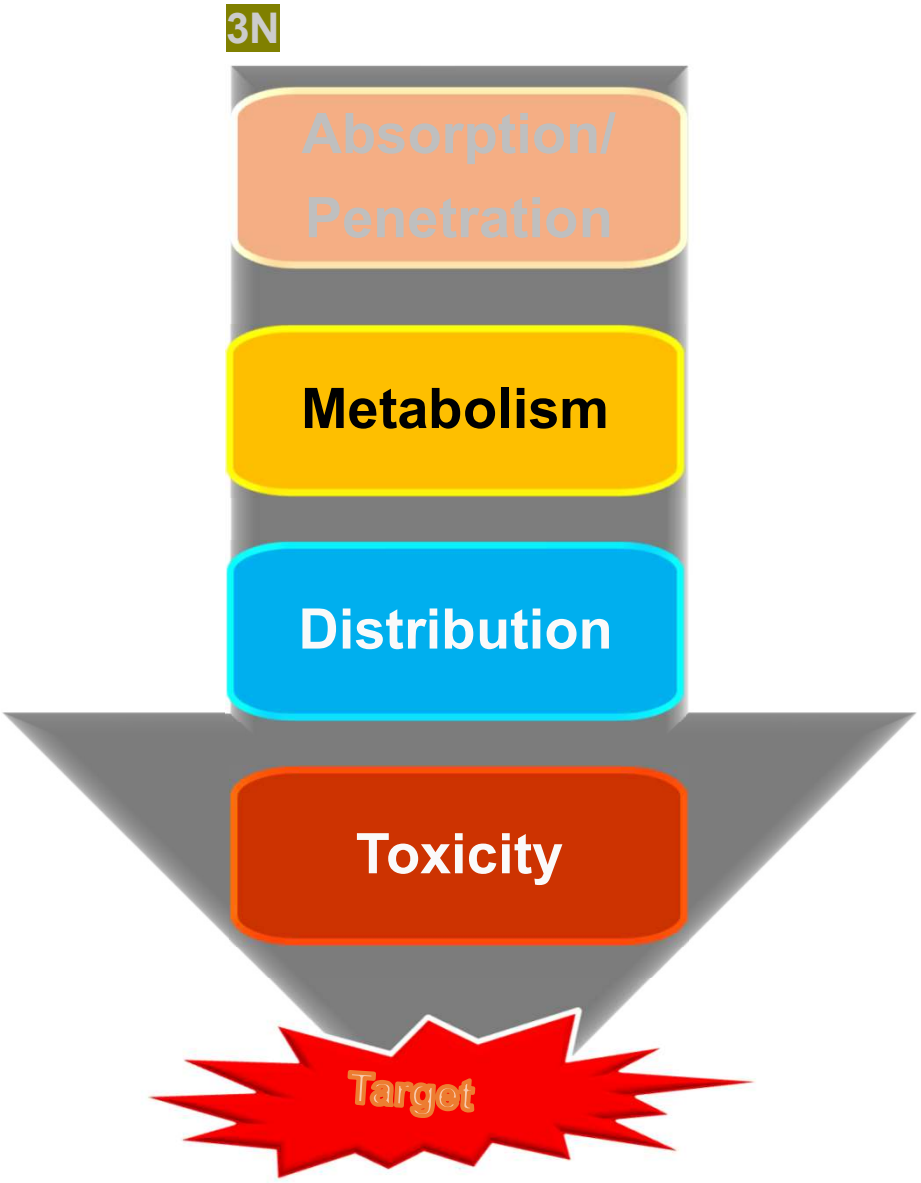
Rank	PDB ID	Target Name	Number of Feature	Fit Score	Normalized Fit Score	z'-score
1	1Q1P	Lactoylglutathione lyase	7	3.789	0.5413	2.95312
2	1EAK	Tyrosine-protein phosphatase non-receptor type 1	6	3.164	0.5273	2.33253
3	2FPY	Dihydroorotate dehydrogenase, mitochondrial	9	3.532	0.3925	2.12106
4	2EA4	Methionine aminopeptidase 2	6	3.128	0.5213	2.09217
5	1XQ0	Carbonic anhydrase 2	4	2.976	0.7441	1.69326
6	1HE4	Flavin reductase	7	2.994	0.4277	1.68684
7	2PDP	Aldose reductase	5	2.976	0.5951	1.57352
8	3D2Y	Retinoic acid receptor RXR-alpha	8	3.386	0.4232	1.57153
9	1FBY	Retinoic acid receptor RXR-alpha	8	3.448	0.431	1.56769
10	1YW9	Methionine aminopeptidase 2	4	2.973	0.7432	1.53514

Rank	PDB ID	Target Name	Number of Feature	Fit Score	Normalized Fit Score	z'-score
1	1POP	Cholinesterase	4	3.716	0.9291	4.55047
2	1KQ0	Methionine aminopeptidase 2	5	3.879	0.7758	4.49728
3	1KON	Chloride intracellular channel protein 1	5	3.763	0.7526	4.18876
4	1V40	Glutathione-requiring prostaglandin D synthase	8	3.709	0.4636	3.82918
5	2OGV	Dipeptidyl peptidase 4	7	3.711	0.5302	3.67607
6	3FLV	Bile acid receptor	8	3.605	0.4506	3.11296
7	1FCX	Retinoic acid receptor gamma	9	3.772	0.4192	2.96597
8	1PQ6	Oxysterols receptor LXR-beta	10	3.777	0.3777	2.90721
9	1FD0	Retinoic acid receptor gamma	8	3.819	0.4774	2.87389
10	1EAK	Tyrosine-protein phosphatase non-receptor type 1	6	3.419	0.5699	2.62568

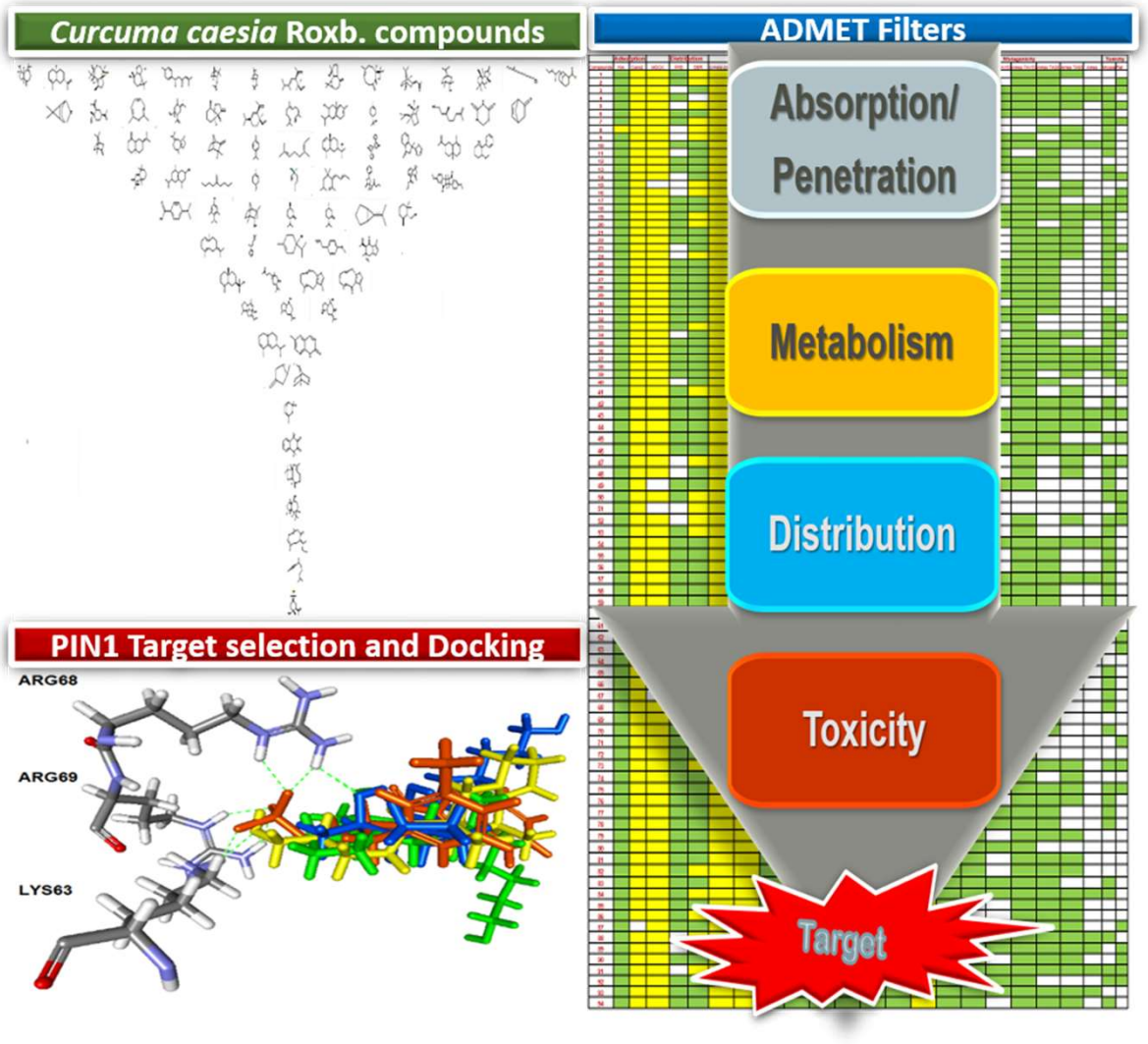
Molecular Docking PIN1 (3ikg) against Lead



Discussion


3N
Absorption/
Penetration
Metabolism
Distribution
Toxicity
Target

Conclusion


Curcuma caesia Roxb. compounds
ADMET Filters
Absorption/ Penetration
Metabolism
Distribution
Toxicity
Target
PIN1 Target selection and Docking
ARG68
ARG69
LYS63

Acknowledgements

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Contact Details

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Thank You

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