



Discovery of TCM Active Ingredients for Malaria Vector Control

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Introduction

Traditional Chinese Medicine (TCM) plays an important role not only in human health, but also in elimination of insects, i.e. mosquito, fruit fly (Fig.1). Indeed, this is the action of ingredients in TCM herbs. Malaria has been raging in tropical developing countries such as Africa, South Asia and South America for a long time, causing great casualties and economic losses. The mosquito is one of key malaria vectors because malaria caused by *Plasmodium falciparum* is mainly transmitted by mosquito bites.



Fig.1 TCM used to treat malaria diseases and kill mosquitos

Chemoinformatics, which can be used in chemical and allied industries in various other forms, is a subject which uses the informatics method and technology to solve complex problems in Chemistry. An in house TCM database (Fig. 2) used to discovery active compounds for malaria vector control and an *in silico* screening platform (Fig. 3) were constructed by its technology.



Fig. 2 In house TCM database

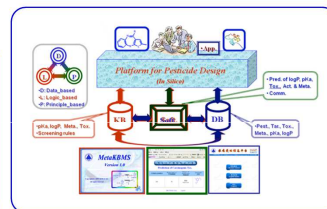


Fig. 3 *In silico* screening platform

Method

There are three methods in Chemoinformatics: Data-based, Logic-based and Principle-based. In this work, the three methods were employed. The TCM database was used to retrieve herbs which have function in eliminating insects, chemical information of ingredients in the herbs. *In silico* screening platform was used to evaluate activity in insecticide, insect repellent, insecticide synergist or insect pheromone of the ingredients (about 25,000 compounds). Three types of toxicity of the ingredients, acute toxicity (rat/oral), mutagenic toxicity (AMES) and carcinogenic toxicity (rat/oral) were also evaluated by the platform.

The "Bottle" method, a kind of tarsal contact assay, was used in this bioassay (Fig. 4).



Fig. 4 "Bottle" bioassay

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Results & Discussion

About 25,000 compounds in herbs were screened by *in silico*, screening platform, then 200 compounds were proposed. Fifty compounds were selected to be bioassayed. At the end, eleven compounds were proposed as active compounds in elimination of mosquitos by bioassayed. The work flow was showed as Fig. 5. The bioassay was finished by China CDC.

The *in silico* and bioassay results of the 10 compounds and the positive control compounds were listed in Table 1.. It is interesting that prediction results of the 3 compounds, SIOC-20201231-2, SIOC-20201231-3 and SIOC-20201231-4, were different from the bioassay results. Their bioassay and *in silico* will be repeated.

Table 1. *In silico* and bioassay results

STR	logP	AT	CT	AMES	Ins. %	IR %	IS %	IP %	DOCK score (best/1000000)	BioAssay Knockdown Activity Rate (%)
SIOC-20200204-4	6.15	4.22	P	P	100	0	0	0	-14.30/-15.04/-10.35	64.44 ± 1.92/100
SIOC-20200924-5	3.01	4.23	P	N	100	0	0	0	-8.55/-9.24/-5.50	12.22 ± 1.92/75.58 ± 6.94
SIOC-20200204-6	2.62	4.1	P	C	22.1	0	0	100	-7.86/-7.91/-6.50	100/100
SIOC-20201231-1	0.98	3.58	P	P	30.3	0	0	0	NULL/-5.47/-7.78	100/100
SIOC-20201231-2	0.40	3.36	N	P	0	0	0	0	NULL/-4.57/-11.63	100/100
SIOC-20201231-3	-0.54	2.27	P	P	0	0	0	0	NULL/-3.13/-12.06	100/100
SIOC-20201231-4	2.68	3.41	P	P	0	0	0	0	-4.65/-4.80/-11.59	1.62/100
SIOC-20201231-5	5.25	4.34	P	N	32.7	0	0	0	-6.41/-6.99/-6.57	71.67/93.33
SIOC-20201231-7	3.69	4.67	P	P	0	80.8	57.7	0	-10.78/-10.55/-12.59	5/100
SIOC-20210226-2	2.09	4.33	N	C(N)	100	0	0	0	-12.85/-13.48/-13.14	100/100
SIOC-20210226-3	2.81	4.41	P	N	100	0	0	0	-5.53/-5.68/-5.91	100/90
Parm.	6.46	3.99	N	C	100	0	0	0	-11.36/-9.79/-11.81	100/100

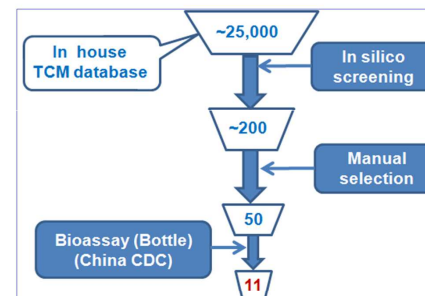


Fig.5 Work flow to get active compounds

Conclusion

All results presented herein showed that combination of *in silico* screening and bioassay is very important in discovery of TCM active ingredients. The two methods can provide information from different sight for researchers during the period of discovery.

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