GANCIDIN W : A POTENTIAL LOW TOXICITY ANTIMALARIAL AGENT ISOLATED FROM ENDOPHYTIC *Streptomyces* SUK10

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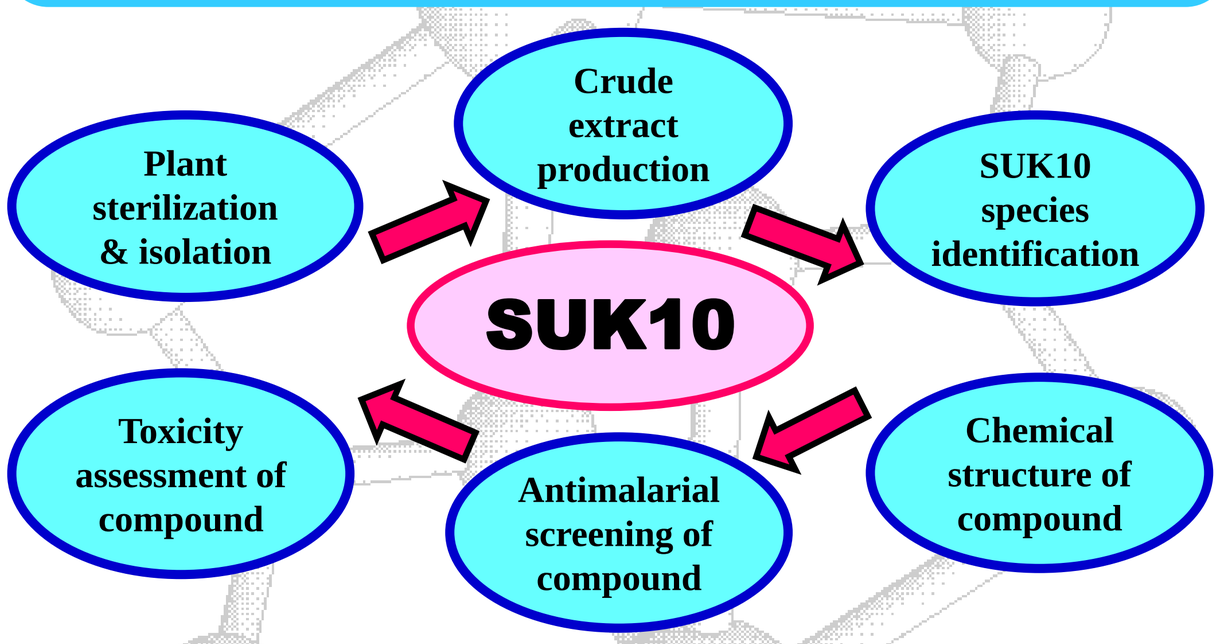
INTRODUCTION

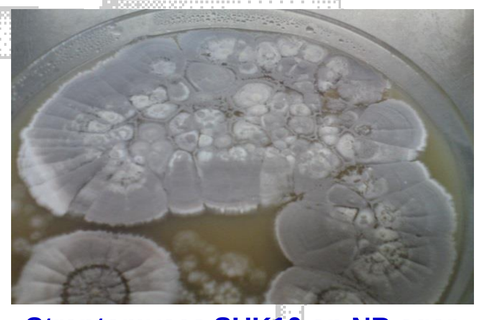
Malaria was reported remained as the most threatening human parasitic disease. In line with this, endophytic *Streptomyces* are potential sources for novel bioactive molecules. In this study, a type of diketopiperazine (DKP) known as Gancidin W (GW, $C_{11}H_{18}N_2O_2$) was successfully isolated from *Streptomyces* SUK10 that inhabited in the bark of *Shorea ovalis*. Using four days suppressive test (4DST), this compound was *in-vivo* tested against *Plasmodium berghei* NK65. At 3.125 µg/kg body weight (bw), there was a significant relationship of ability to inhibit the growth of *P. berghei* NK65 when GW exhibited an inhibition rate of nearly 80% on male ICR strain mice. Comparing with quinine hydrochloride and 0.9% normal saline as the controls, 50% of the mice in this group was managed to survive more than 230 days. Although ALT and AST level was slightly higher, there was no abnormalities were found on the tested organs. These findings indicated that GW isolated from *Streptomyces* SUK10 exhibited very low toxicity and is a good candidate as a potential antimalarial agent.

METHODOLOGY

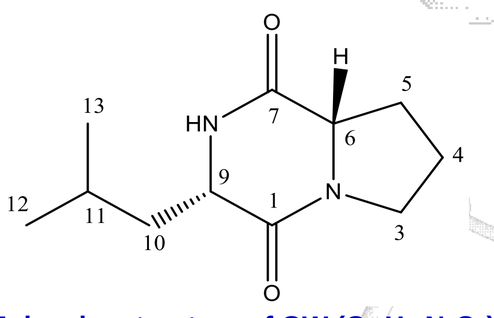


RESULTS

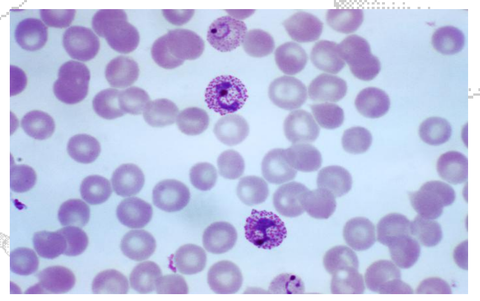
Shorea ovalis tree



Streptomyces SUK10 on NB agar



Molecular structure of GW ($C_{11}H_{18}N_2O_2$)

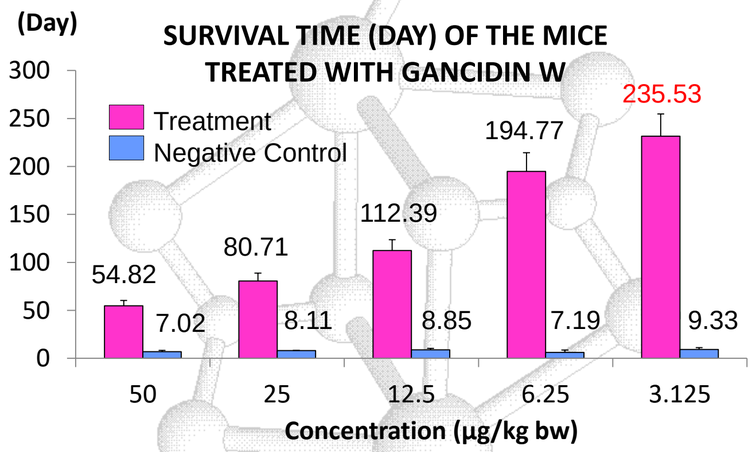


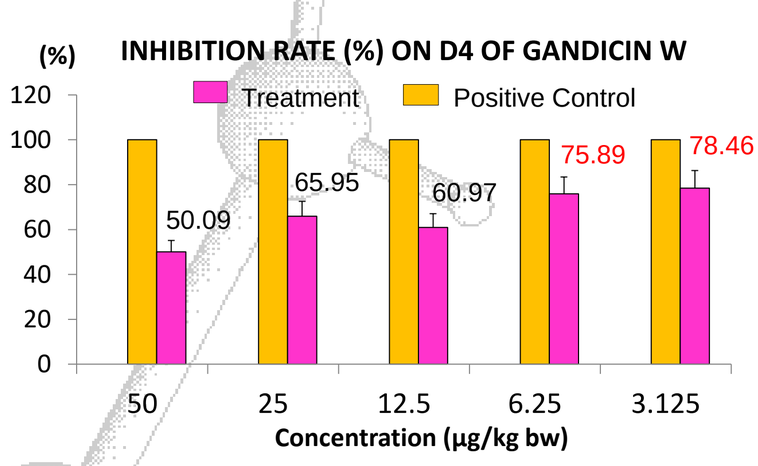
P. berghei-infected RBC

Sacrificed mice for toxicity tests

BIOCHEMICAL TEST FOR ALT, AST, ALP AND STP IN TOXICITY ASSESSMENT

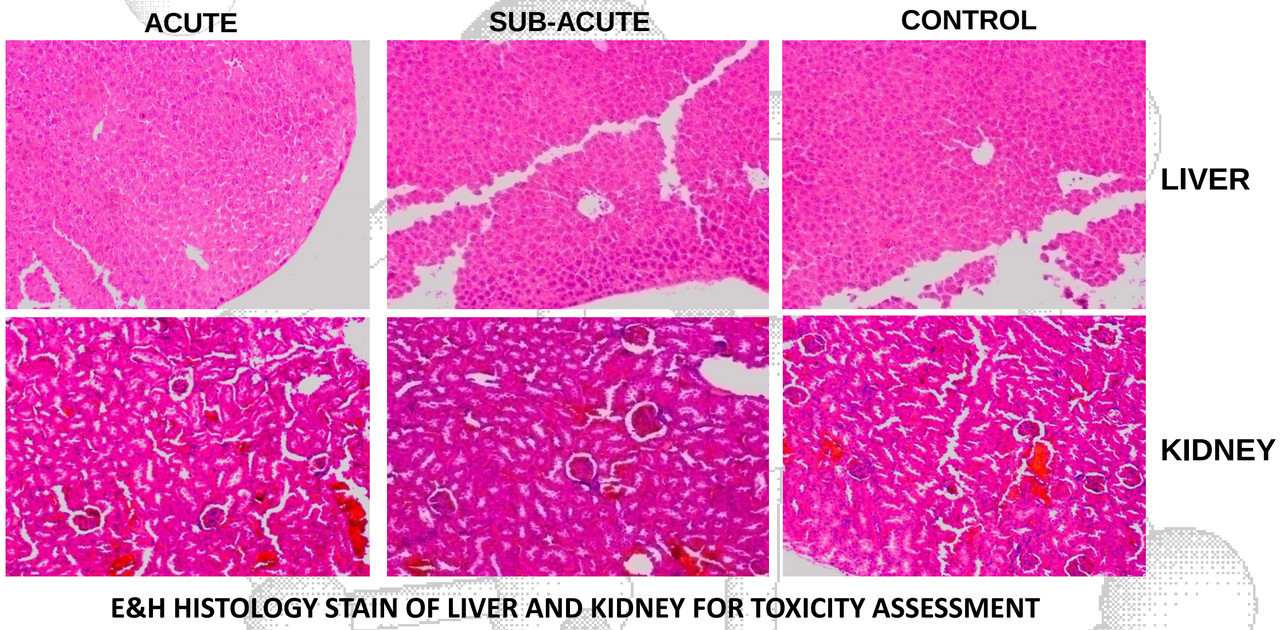
Test	TA	TB	TC	TD	CN	CI	NR	Unit
ALT	41.81 ± 2.14	45.20 ± 1.13	67.57 ± 2.91	**94.03 ± 2.02**	41.03 ± 3.91	44.83 ± 1.11	40 – 93	IU/L
AST	133.13 ± 2.04	125.93 ± 2.12	167.76 ± 2.27	**209.01 ± 2.09**	111.62 ± 1.19	134.43 ± 4.01	92 – 206	IU/L
ALP	62.76 ± 2.33	59.4 ± 2.97	69.2 ± 2.90	68.03 ± 2.10	61.46 ± 2.46	58.32 ± 2.97	54 – 115	IU/L
STP	6.12 ± 2.32	7.21 ± 3.81	7.93 ± 2.01	8.83 ± 3.90	6.40 ± 1.01	6.80 ± 3.06	5.8 – 9.5	g/dL





DISCUSSION

- GW give very low toxicity and unpleasant effects, make them as a potential candidate for antimalarial drug and offer a promising way to treat malaria
- GW was within polyketide and DKP clustered in which most of current antimalarial drugs were belongs and characterized.
- Until current, antimalarial property of GW was never yet being revealed.
- All mice (n=6) treated with 6.25 µg/kg bw GW were managed to survive up to almost their normal lifespan.
- GW was isolated from *Streptomyces* SUK10 and not from plants, make them sustainable for up-scaled production through bioreactor.
- Suggestion : (a) Mechanism of action of GW, (b) Full genome characteristic of *Streptomyces* SUK10, and (c) *In-vitro* antimalarial assessment of GW



E&H HISTOLOGY STAIN OF LIVER AND KIDNEY FOR TOXICITY ASSESSMENT

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CONCLUSION

Gancidin W isolated from *Streptomyces* SUK10 is a very good bioactive property and a potential substance as an anti-malarial agent.

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