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in vitro activity of *Andrographis paniculata* (Burm.f.) Wall.ex Nees leaves ethanolic extract inhibits host cell invasion and intracellular replication of *Toxoplasma gondii* via modulation of *Protein kinase G* (PKG)

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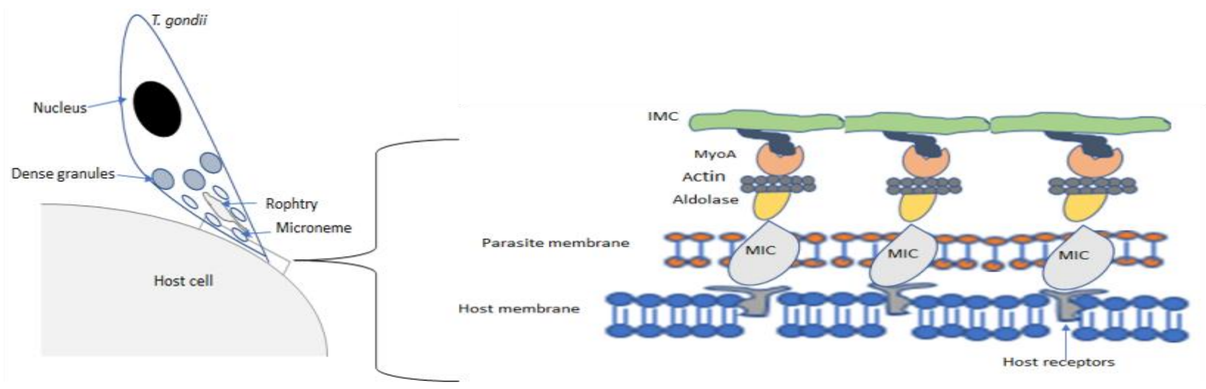
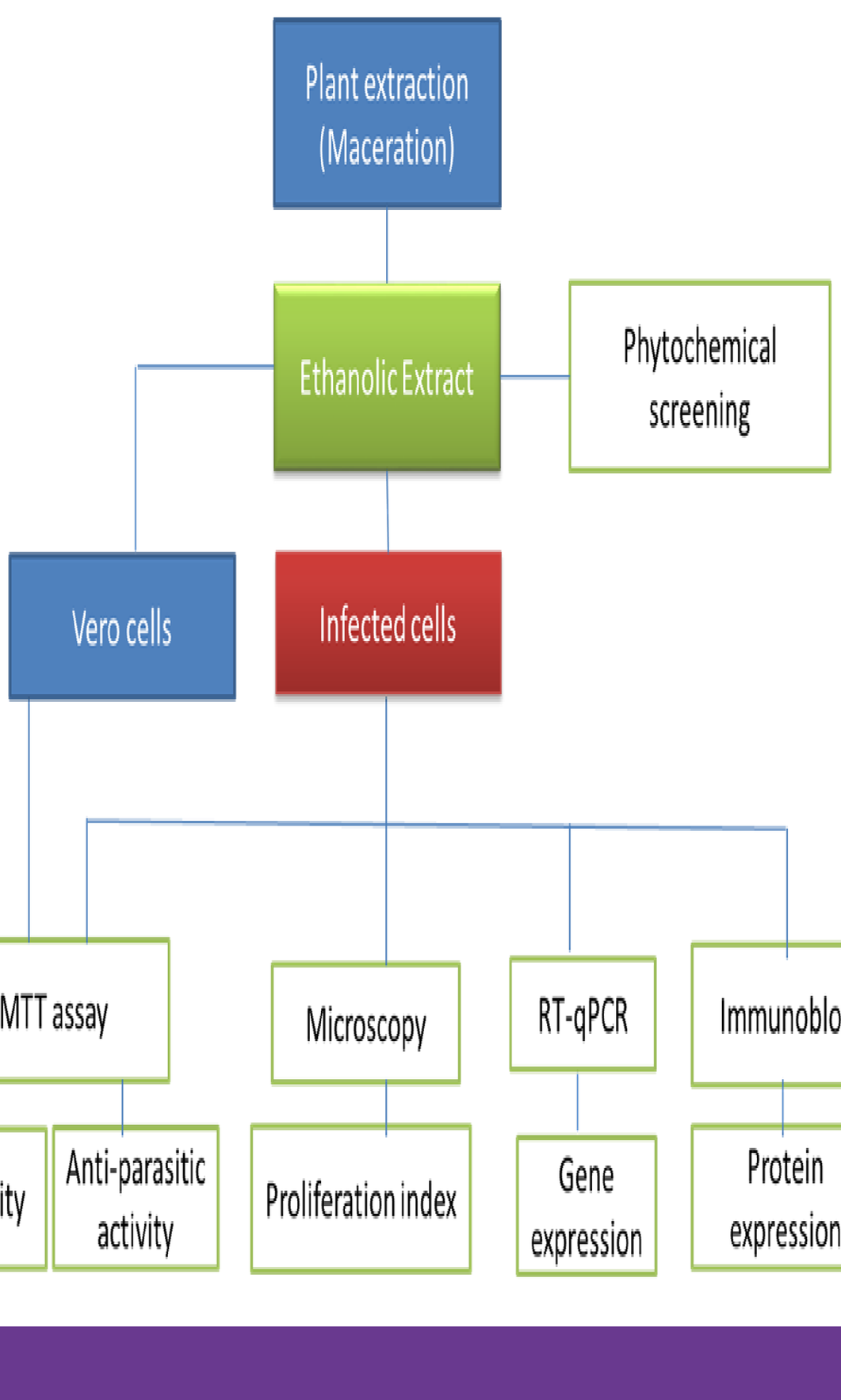
INTRODUCTION & AIM

Toxoplasmosis remains globally relevant because of its consequences on pregnancy outcomes, mental disorders, and opportunistic tendencies in immunocompromised individuals. Current medications have severe side effects on the host, low efficacy against the parasites, and potential development of resistance. This emphasizes the need to discover better and safer drugs to treat toxoplasmosis. This study evaluated the in vitro effects of ethanolic leaf extracts of *Andrographis paniculata* (EEAP) on protein kinase G (PKG) involved in cell invasion by *T. gondii*.



METHOD



RESULTS & DISCUSSION

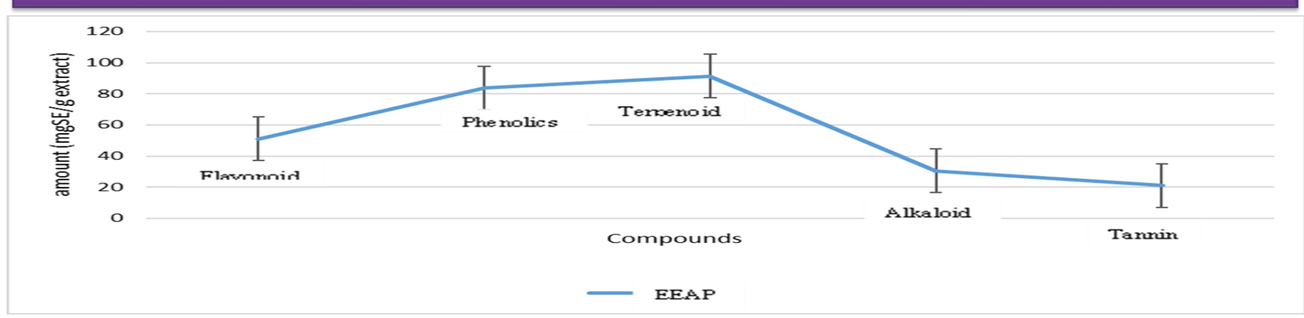


Table 1. IC_{50} concentrations and selectivity index

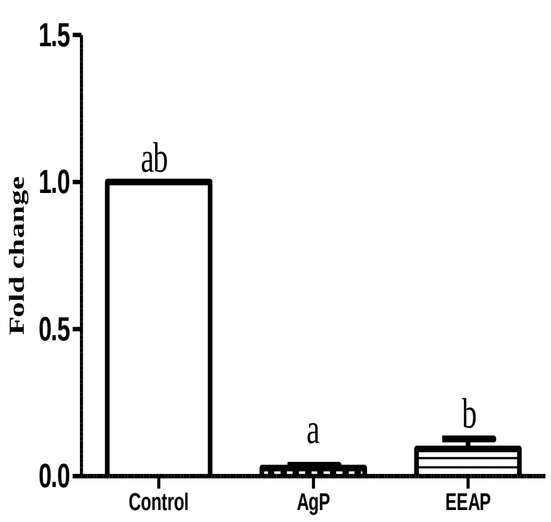
Extract/compound	Cytotoxicity[e] (IC_{50}) µg/mL	Anti-parasitic[f] (IC_{50}) µg/mL	Selectivity index SI= e/f)
Clindamycin	116.00 ±2.3[a, b, c]	8.31 ±1.04[a, c]	13.9
Andrographolide	179.00 ±1.5 [a, b]	6.31±1.4 [b]	28.4
EEAP	142.50 ±1.2 [a, c]	4.36±1.43 [a, c]	32.7

Note: IC_{50}: 50% inhibitory concentration, Selectivity index (SI) is calculated as the ratio of the IC_{50} concentration obtained in cytotoxicity assay (e) for each compound to the IC_{50} concentration obtained in anti-parasitic assay (f) given as (e/f). High SI indicates that extract has more activity on the parasite and safer on the host cells. Means with the same letters differ significantly P<0.0001.

Table 2. Assessment of proliferation index in 4 h post-infection treatment model

	24 h after treatment			
compounds	Infection index	% inhibition	Intracellular proliferation	% inhibition
Negative control	81.67 ±2.1[a, b, c]	-	150.30 ±2.2[a, b, c]	-
Clindamycin	60.67 ±1.7 [a, b, c]	25.71	104.00 ±1.5 [a,b ,c]	30.81
Andrographolide	21.67 ±1.0 [a, b]	73.47	69.67 ±2.6 [a, b]	53.65
EEAP	27.33 ±1.8 [a, c]	66.54	74.33 ±2.11[c]	50.55

Note: The data for the infection index and intracellular replication is the Mean ± SD of the total values obtained in triplicate of three independent assays in every 200 examined cells. The percentage inhibition represents the inhibition of either parameter by the compound in relation to negative control whose inhibition corresponds to 100%. Means with the same letters differ significantly at P<0.0001.



TgPKG expression normalized to *Tgβ-tubulin.*
EEAP: Ethanolic extract of Andrographis paniculata, AgP: Andrographolide
a & b significantly different (P=0.002)from ab

MIC1	Treatment	Normalized values	Fold change	SEM
4 h post-infection	EEAP	0.0670	0.6982	0.2509
	AgP	0.0693	0.6971	0.1386
	Control	0.1010	1.0000	0.0000
P-value		0.03546	0.03882	

MIC2	Treatment	Normalized values	Fold change	SEM
4 h post-infection	EEAP	0.1584	0.2856	0.0610
	AgP	0.1973	0.3558	0.1285
	Control	0.5546	1.0000	0.0000
P-value		0.0001	0.0001	

CONCLUSION

This study showed that EEAP and andrographolide are promising drug candidates effective against *T. gondii*, safe for the host cells, and can be used for the development of a potent anti-Toxoplasma drug to target the *TgPKG* gene involved in cell invasion to prevent disease progression.

FUTURE WORK / REFERENCES

REFERENCES

1. Lebrun, M., Carruthers, V. B, and Cesbron-Delauw, M. F. (2014). *Toxoplasma* secretory proteins and their roles in cell invasion and intracellular survival. In *Toxoplasma gondii* (pp. 389-453). Academic Press.