In vitro evaluation of trypanocidal efficacy of benzyltriazole derivatives on *Trypanosoma evansi*

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NWU

Animal Trypanosomosis

- Surra

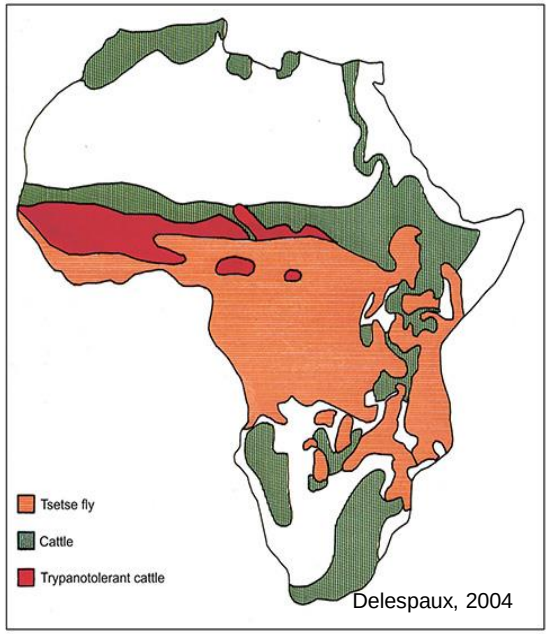
Causative agent: *Trypanosoma evansi*

Host: Infects livestock and potentially a human pathogen

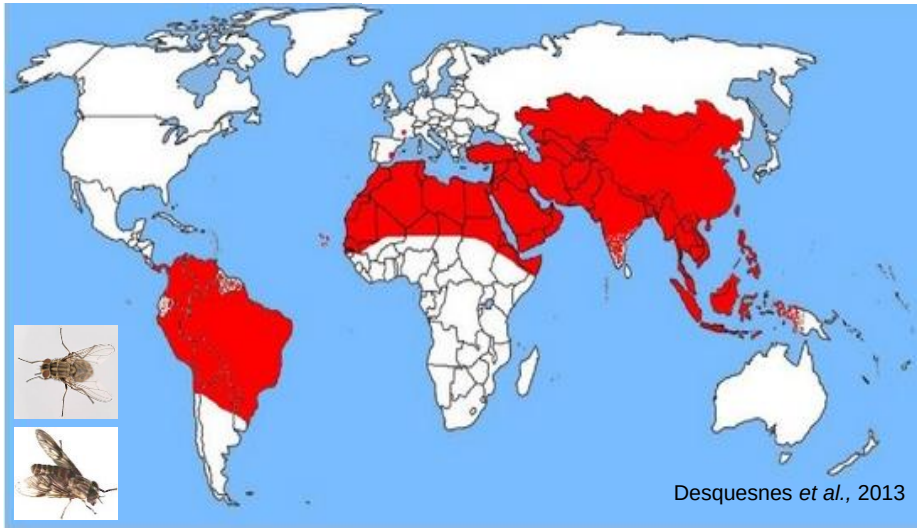
- Horses, camels, donkeys, cattle and buffaloes

Distribution: North Africa, South America & Asia

Mechanical transmission: Blood-sucking insects, especially *Tabanus* and *Stomoxys* (OIE, 2010)



Delespaux, 2004


Desquesnes *et al.*, 2013

Impact of surra

Agricultural and animal husbandry sector:

- Distorted draught power
- Reduced productivity
- Reduced manure production
- Immunosuppression livestock

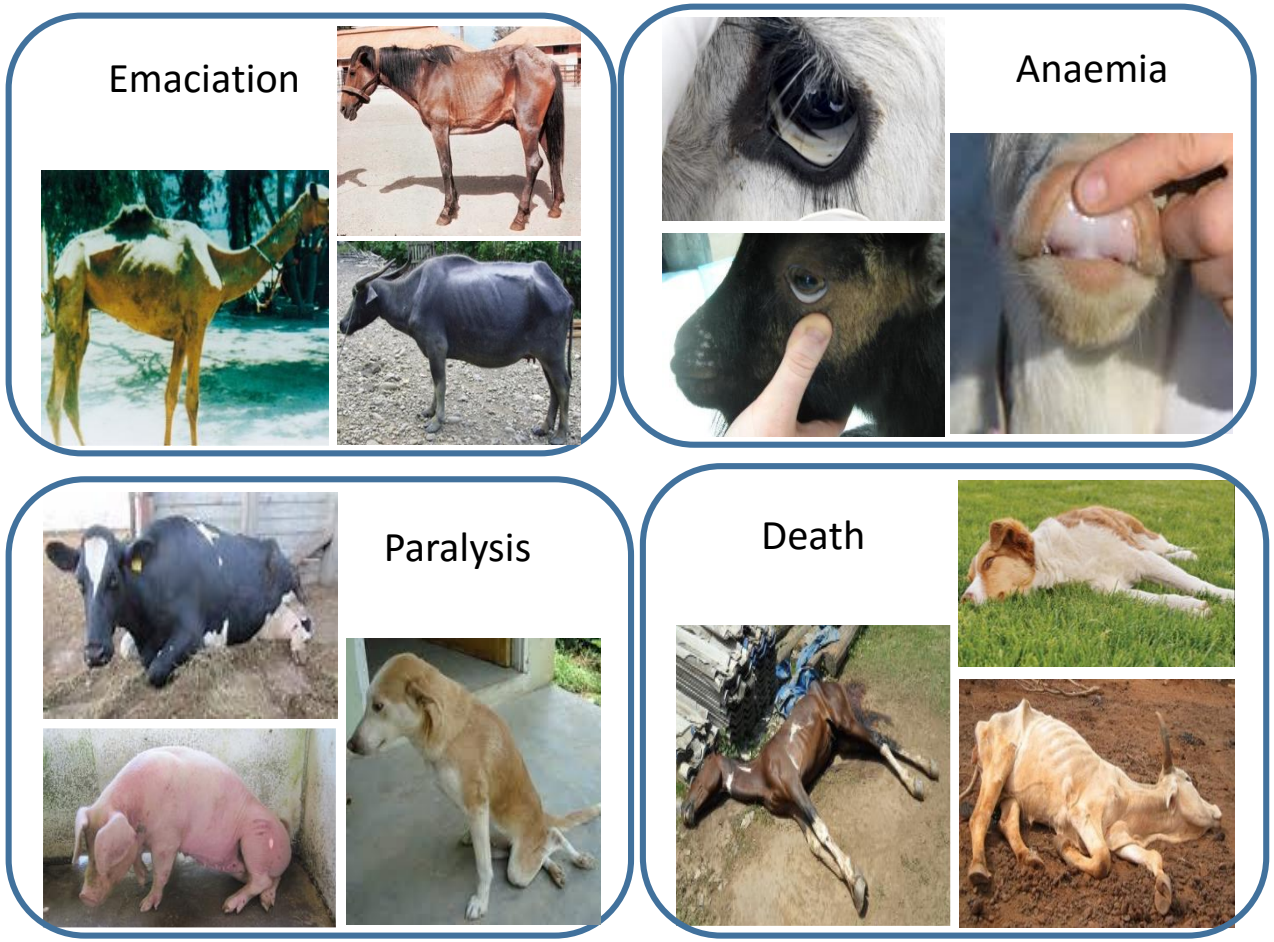
Affected countries:

- Africa, South America and South-East Asia

Economic losses (Desquesnes *et al.,* 2013):

- US$158,000/year

Clinical signs



Dargantes *et al.*, (2005); Desquesnes *et al.*, (2013); Diseaseinafrica.com (2015)

Control and treatment

Therefore, a search for novel compounds still continues

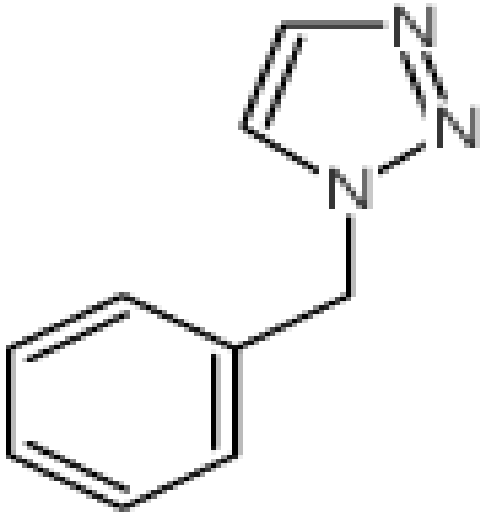
- Less toxic
- Tolerable by the hosts
- Better pharmacokinetics

Trypanocidal drugs

- Tolerance of the drugs by the hosts
- Toxicity
- Extended withdrawal periods
- Chemo-resistance

Benzyltriazole

Heterocylic compound containing three nitrogen atoms fused to a benzene ring



Benzyltriazole (Suma *et al.,* 2011; Ren *et al.,* 2014)

- Low toxicity
- Few side effects
- Good water solubility
- Promising bioavailability
- Diversity of drug administration

Effective pharmacological properties (Khabnadideh *et al.,* 2012; Briguglio *et al.,* 2015):

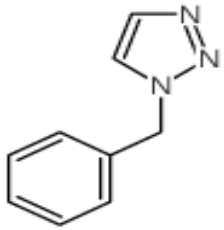
- Antibacterial, antifungal, antiviral, and analgesic

Objective

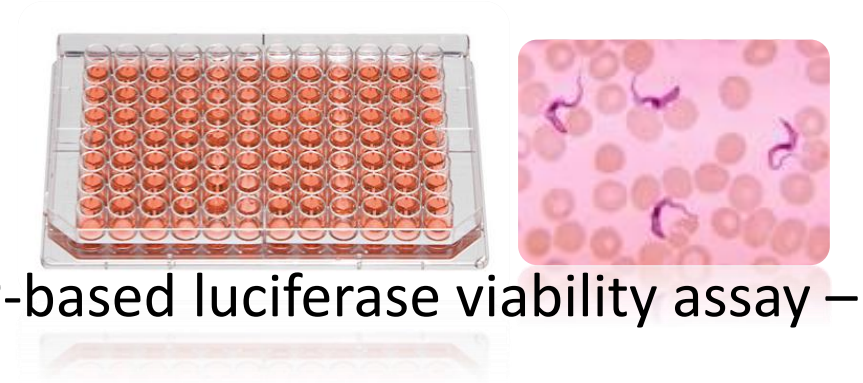
To evaluate the effects of benzyltriazole derivatives on *Trypanosoma evansi, in vitro.*

In vitro tests

25 Benzyltriazole derivative compounds



In vitro trypanocidal effects (Suganuma *et al.,* 2014):



ATP-based luciferase viability assay – *T. evansi*

- Final concentration: 25 µg/mL

- Data analysis - IC_{50} values

GraphPad

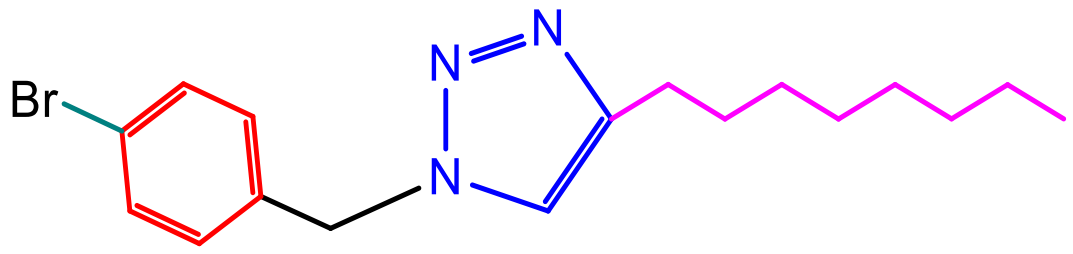
Results

No.	Compound identity	IC_{50} (µg/ml) ± S.D
1	NWU_FJS_001	-
2	NWU_FJS_002	-
3	NWU_FJS_003	18,86 ± 1,37
4	NWU_FJS_004	-
5	NWU_FJS_005	24,09 ± 0,44
6	NWU_FJS_101	23,41 ± 1,05
7	NWU_FJS_102	12,84 ± 0,21
8	NWU_FJS_103	7,55 ± 0,39
9	NWU_FJS_104	-
10	NWU_FJS_105	-
11	NWU_FJS_201	-
12	NWU_FJS_202	22,47 ± 0,50

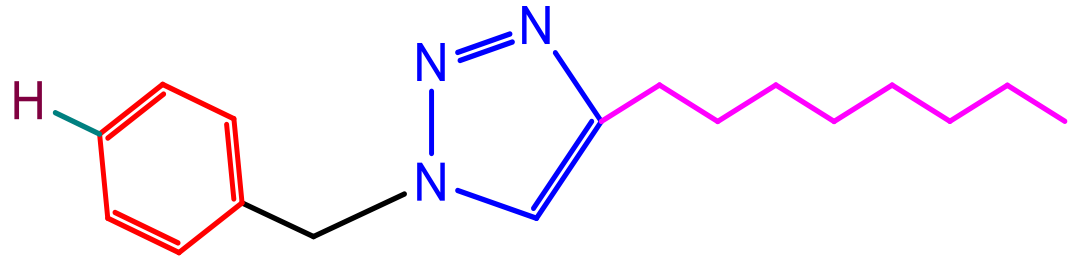
Diminazene aceturate: 0.32 µg/ml as a positive control

No.	Compound identity	IC_{50} (µg/ml) ± S.D
13	NWU_FJS_203	8,16 ± 0,79
14	NWU_FJS_204	18,96 ± 1,37
15	NWU_FJS_205	-
16	NWU_FJS_301	-
17	NWU_FJS_302	20,94 ± 0,82
18	NWU_FJS_303	21,89 ± 1,36
19	NWU_FJS_304	-
20	NWU_FJS_305	-
21	NWU_FJS_401	5,61 ± 0,39
22	NWU_FJS_402	1,49 ± 0,49
23	NWU_FJS_403	5,10 ± 0,68
24	NWU_FJS_404	-
25	NWU_FJS_405	-

Results



NWU-FJS-103



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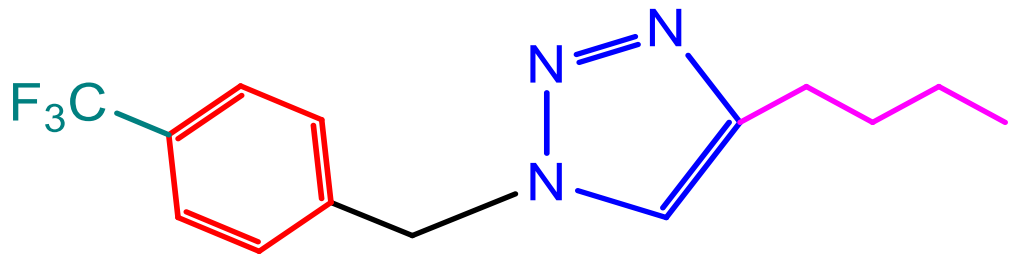

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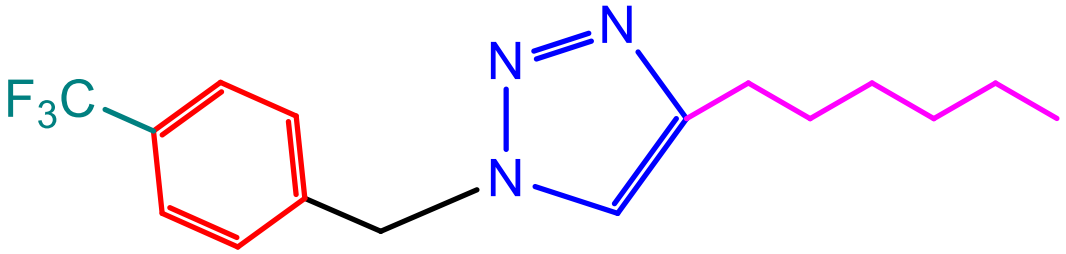
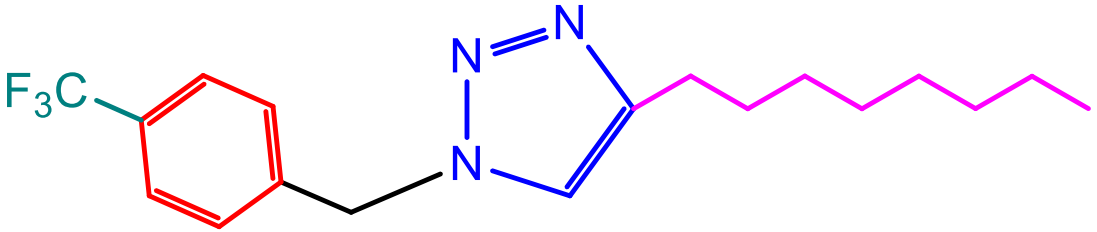


NWU-FJS-402



NWU-FJS-403

Discussion

Obtained IC_{50} values for the compounds were higher than the standard drug used, diminazene aceturate (0.32 µg/ml).

Zhang *et al.* (1993), documented the IC_{50} values for standard commercial drugs for *T. evansi,* stated that *in vitro* result do not necessarily interpret *in vivo* results.

According to Nwaka and Hudson (2006), the criteria for drug candidates for African trypanosomiasis: IC_{50} <1 µM; selectivity >100.

Discussion

Functional groups play a significant role in the efficacy of compounds (Burugulgio *et al.,* 2015).

Slight modification of the substituents and/or functional groups improved medicinal activity of the benzyltriazole compounds and resulted in less adverse effects.

At 50 µg/mL epimastigotes and trypomastigotes form of *T. cruzi* were inhibited.

Antitumor effects and athelminitic activity.

Conclusion

The study has documented three compounds eligible for the further studies on the treatment of *T. evansi*

Future plans

Assessing the cytotoxicity and toxicity effects of the compounds

In vivo efficacy of the compounds will be determined in mice

Acknowledgements

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Thank you for your kind attention