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## Design, synthesis and biological evaluation of hybrid bioisoster derivatives of hydrazone and nitric oxide releasing groups with potential and selective anti-*Trypanosoma cruzi* activity

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Hybrid bioisoster derivatives from N-acylhydrazones and furoxan groups were designed with the objective of obtaining at least a dual mechanism of action: cruzain inhibition and nitric oxide (NO) releasing activity. Fifteen designed compounds were synthesized varying the substitution in N-acylhydrazone and in furoxan group as well. They had its anti-*Trypanosoma cruzi* activity in amastigotes forms, NO releasing potential and inhibitory cruzain activity evaluated. The two most active compounds both in the parasite amastigotes and in the enzyme contain the nitro group in *para* position of the aromatic ring. The permeability screening in Caco-2 cell and cytotoxicity assay in human cells were performed for those most active compounds and both showed to be less cytotoxic than the reference drug, benznidazole. Also molecular modeling approach was used to find the molecular properties that more influenced the biological activity and to evaluate the interaction with the molecular target cruzain. Compound containing nitro group in *para* position was the most promising, since besides activity it showed good permeability, selectivity index, higher than the reference drug and also showed no significant changes in human cells in studies of DNA fragmentation and cell cycle. Thereby this compound was considered a promising compound for further *in vivo* studies. Nevertheless optimization in its structure has been carry out to improve the pharmacodynamics and pharmacokinetics properties.

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## Open Dialogue as a contribution to a healthy society: Threat or chance?

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Open Dialogue is a post modern approach to severe crises in mental illness and has been developed in Finland since the early 80ties of the last century. Y. Alanen from the University of Turku together with his team created the Need Adapted Treatment, which later has been further developed mainly by Jaakko Seikkula and the team of the Keropoudas Hospital in Tornio in Western Lapland. It promotes an early intervention by involving the family and the network of a patient at once, uses best practices of systemic therapies, integrates other professions and peers, uses low dose medication and shared decision making within the network. It is a very comprehensive change in organizational aspects of the treatment system going along with it. It needs a different way of financing and reduces inpatient treatment in the long run. And that is where the risks are: Medication is not at the core interest any more, outpatient treatment is vastly in favor, hospitals would have to close beds, doctors and psychologists are no longer the all knowing persons, everybody is an expert of his own life. People interested in this approach gather in the annual meeting of The International Network For The Treatment of Psychosis, founded in 1996. Participants come mainly from scandinavian countries and Finland, Germany, Poland, Lithuania and nowadays from the UK and the US.

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