

LETTER TO THE EDITOR

Open Access

Anti-oxidative trypanocidal drugs, myth or reality

Soodabeh Saeidnia

Sir,

"Blueberries best be eaten because they taste good, not because their consumption will lead to less cancer." Prof. Jim Watson [1].

Recently, Professor Jim Watson, father of DNA double-helix, has described in his paper that antioxidant supplements may have caused more cancers than they have prevented. Alongside this controversial, several papers give rise on looking for anti-cancers among antioxidants [2-4]. In reality, mechanism of anti-cancer action is very important, where induction of free radicals and augmentation of Reactive Oxygen Species (ROS) are the main pharmacological modes of anti-neoplastic activity [5]. In spite of the fact that beneficial role of antioxidants in chemoprevention of cancer has been well-known, effectiveness of them in treatment of cancer is still in challenge.

Interestingly, there is a similar situation for another important disease, Chagas (American trypanosomiasis), a tropical parasitic illness caused by the flagellate protozoan *Trypanosoma cruzi* and affects eight to 10 million people residing in Latin American countries [6,7]. Nowadays natural compounds have been evaluated for discovery of new chemotherapeutics in treatment of Chagas disease. But, literature revealed that most of the researchers select the compounds without attention to their probable antioxidant activity, while therapeutic action of the remarkable trypanocidal compounds like elatol involves mitochondria as the primary target leading to increase of ROS generation through the electron transport chain, which consequently affects cell membrane and DNA integrity and finally death of parasite [8]. Although this is not the only mechanism of action for trypanocidal drugs, well-known natural phenolics such as gallic acid can act *via* pro-oxidant activity as well as enhancing DNA single-strand breaks to kill *Trypanosoma* [9]. Furthermore, anti-trypanosoma activity of komaroviquinone (a diterpenoid) was found to be attributed by generation of ROS catalyzed by *T. cruzi*

old yellow enzyme [10]. It seems that potent natural antioxidants like hydroxycoumarins derivatives or flavonoids are not potentially strong trypanocidal agents [11].

The question arise from this concept is "why does a physician recommend consumption of antioxidant in treatment of trypanosomiasis?" The answer to this question may be hidden behind the differences in mechanism of actions for trypanocidal drugs and also the role of antioxidants in prevention of inflammation in this illness. To the best of our knowledge, consumption of antioxidant supplements is new perspective in therapy of Chagas disease because of the attenuation of oxidative stress associated to this disease [12]. Additionally, it has been reported that *Trypanosoma* infection decreases the levels of reduced glutathione (GSH) in the blood, liver, kidney, and also the plasma levels of vitamin C [13]. For this reason, they believe that supplementation of infected patient with vitamin C could prevent the depletion of endogenous antioxidants. Actually, another probable reason for this entrenched attitude is the ubiquitous application of antioxidant supplements. Therefore, we recommend the researchers to focus on possible mode of actions for trypanocidal candidates, especially when the nominated compounds are proved to possess antioxidant ability.

Competing interest

The author declared that there is no competing interest.

Received: 4 March 2013 Accepted: 8 March 2013

Published: 12 March 2013

References

1. Watson J: Oxidants, antioxidants and the current incurability of metastatic cancers. *Open Biology* 2013. doi:10.1098/rsob.120144. online Jan 8.
2. Abdollahi M, Shetab-Boushehri SV: Is it right to look for anti-cancer drugs amongst compounds having antioxidant effect? *DARU* 2012, **20**:61.
3. Saeidnia S, Abdollahi M: Who plays dual role in cancerous and normal cells? Natural antioxidants or free radicals or the cell environment. *Int J Pharmacol* 2012, **8**:711-712.
4. Shetab-Boushehri SV, Abdollahi M: Current concerns on the validity of in vitro models that use transformed neoplastic cells in pharmacology and toxicology. *Int J Pharmacol* 2012, **8**:594-595.
5. Wiwanitkit V, Chaiyasit K: Antioxidant as an anticancer: consideration. *DARU* 2012, **20**:96.
6. Saeidnia S, Gohari AR, Uchiyama N, Ito M, Honda G, Kiuchi F: Two new monoterpene glycosides and trypanocidal terpenoids from *Dracocephalum kotschy*. *Chem Pharm Bull* 2004, **52**:1249-1250.

Correspondence: saeidnia_s@tums.ac.ir
Medicinal Plants Research Center, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran 1417614411, Iran

7. Saeidnia S, Gohari AR: **Trypanocidal monoterpenes: lead compounds to design future trypanocidal drugs.** In *Studies in natural product chemistry*. Volume 37th edition. Edited by Rahman A. Netherland: Elsevier; 2012:173–189.
8. Desoti VC, Lazarin-Bidóia D, Sudatti DB, Pereira RC, Alonso A, Ueda-Nakamura T, Dias Filho BP, Nakamura CV, Silva Sde O: **Trypanocidal action of (-)-elatol involves an oxidative stress triggered by mitochondria dysfunction.** *Mar Drugs* 2012, **10**:1631–1646.
9. Nose M, Koide T, Morikawa K, Inoue M, Ogihara Y, Yabu Y, Ohta N: **Formation of reactive oxygen intermediates might be involved in the trypanocidal activity of gallic acid.** *Biol Pharm Bull* 1998, **21**:583–587.
10. Uchiyama N, Kabututu Z, Kubata BK, Kiuchi F, Ito M, Nakajima-Shimada J, Aoki T, Ohkubo K, Fukuzumi S, Martin SK, Honda G, Urade Y: **Antichagasic activity of komaroviquinone is due to generation of reactive oxygen species catalyzed by Trypanosoma cruzi old yellow enzyme.** *Antimicrob Agents Chemother* 2005, **49**:5123–5126.
11. Pérez-Cruz F, Serra S, Delogu G, Lapier M, Maya JD, Olea-Azar C, Santana L, Uriarte E: **Antitrypanosomal and antioxidant properties of 4-hydroxycoumarins derivatives.** *Bioorg Med Chem Lett* 2012, **22**:5569–5573.
12. Maçao LB, Wilhelm Filho D, Pedrosa RC, Pereira A, Backes P, Torres MA, Fröde TS: **Antioxidant therapy attenuates oxidative stress in chronic cardiopathy associated with Chagas' disease.** *Int J Cardiol* 2007, **123**:43–49.
13. Eghianruwa KI: **The effect of supplemental antioxidants vitamin C and dimethyl sulfoxide on weight gain and survival in T. brucei infected and diminazene treated rats.** *Veterinarski Arhiv* 2012, **82**:519–529.

doi:10.1186/2008-2231-21-21

Cite this article as: Saeidnia: Anti-oxidative trypanocidal drugs, myth or reality. *DARU Journal of Pharmaceutical Sciences* 2013 **21**:21.

Submit your next manuscript to BioMed Central and take full advantage of:

- Convenient online submission
- Thorough peer review
- No space constraints or color figure charges
- Immediate publication on acceptance
- Inclusion in PubMed, CAS, Scopus and Google Scholar
- Research which is freely available for redistribution

Submit your manuscript at
www.biomedcentral.com/submit

