



Mithradate's antidote : An antique nanomedicine ?

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Introduction: Mithradate VI Eupator of Pontus¹ was born on 135 BC and his antidote against poisoning is certainly the main reason why his name crossed centuries, as it was still reported in the 19th century European Pharmacopeia². Despite an unknown exact composition, Celsus's recipe (38 ingredients)³ can be taken as the closest preparation of Mithradate's antidote⁴. An intriguing constituent is the Lemnian Earth. From our 21st century point of view, this presence should discredit the entire preparation, especially with the Hephaistos mythology around this island and with the ceremonial around the collection of the earth, occurring just once a year with a final presentation as an Artemis sealed-stamped tablet⁵. Nevertheless, from a chemical point of view the tablets could have been composed of montmorillonite, kaolin, alum and hematite⁵, with respective percentages of 40, 35, 20 and 5 and therefore be a source of aluminium which, reacting with organic molecules could have led to aluminium nanoparticles synthesized using a green process⁶. Our work aims to demonstrate that Mithradate may have unintentionally synthesized aluminium nanomedicines boosting the antidote effect of the formulation.

Results: After oxalic and malic acid (brought in the antidote via rheum) incubation with montmorillonite powder, aluminium ions could be quantitatively extracted. Addition of crocin, one of the organic compounds present in the antidote, led to the green synthesis of aluminium oxide particles with a diameter of 1075±250 nm as characterized by MEB-EDX.

Conclusions: Mithradates' antidote could have contained aluminium oxide nanoparticles that may have positively impacted the anti-poisoning effect of the preparation: indeed, those particles are described as efficient detoxifying systems for arsenite⁷ or peptidic based toxin⁸.

References

- [1] Mayor A. The Poison King: The Life and Legend of Mithradates, Rome's Deadliest Enemy (2011).
[2] Norton, S. The pharmacology of Mithridatum: (2006). [3]Celsus, A. C. *Medicinae Libri*. [4] Totelin, L. *Early Science and Medicine* 1–19 (2004). [5]Hall, A. J. & Photos-Jones. *Archaeometry* 50, 1034–1049 (2008). [6] Ansari, M. A. *et al. World Journal of Microbiology and Biotechnology* 31, 153–164 (2015). [7] Prabhakar, R. & Samadder, S. R. *Journal of Molecular Liquids* 250, 192–201 (2018). [8] Jones, L. S. *et al.. Journal of Biological Chemistry* 280, 13406–13414 (2005).