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学位論文内容の要旨

博士の専攻分野名称：博士（農学）

氏 名：Khine Swe Nyunt

学位論文題名

Isolation of Antitrypanosomal Compounds from Myanmar Medicinal Plants

(ミャンマー薬用植物からの抗トリパノソーマ剤の探索)

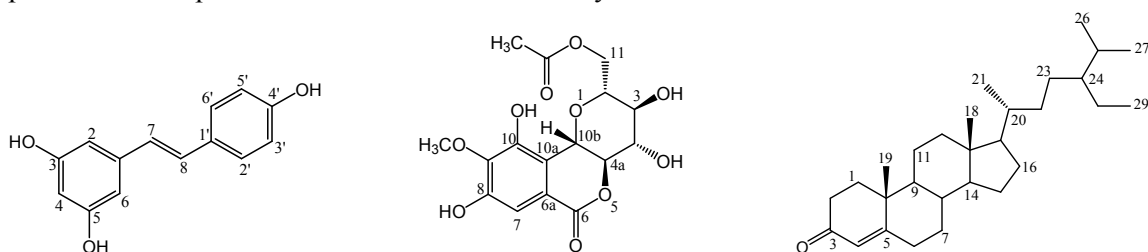
Introduction

Trypanosomiasis, a serious parasitic disease affecting humans and animals in many countries, is caused by blood-dwelling *Trypanosoma* species. The genus *Trypanosoma* is divided into two main groups based on the mode of transmission by their insect vectors: stercoraria and salivaria. Among of the salivarian trypanosomes, *Trypanosoma evansi* has the widest distribution of all species of trypanosomes and the greatest range of mammalian hosts, making it one of the most economically important protozoan diseases present in the world today. *T. evansi* is an animal-pathogenic flagellated protozoan parasite. It infects a variety of animals and causes epidemics of a disease known as surra. The disease occurs not only in Africa, but also in Central and South America and Asia. The parasites are mechanically transmitted by biting hematophagous insects, especially flies in the Tabanidae family such as horseflies (*Tabanus* spp.) and stable flies (*Stomoxys* spp.) from one infected host to other. Some antitrypanocidal drugs reduce the severity of clinical signs and the mortality associated with the disease. However, several problems are associated with these drugs due to their side effects and ineffectiveness against drug resistant parasites in many regions. Therefore, an alternative chemotherapeutic agent with fewer side effects is urgently needed to prevent and treat disease caused by *Trypanosoma* species. Medicinal plants play a key role in world for health, since they are sources of many pharmacologically active compounds. Myanmar is abundant in plant resource, and Myanmar traditional medicinal practitioners have been using a variety of herbal preparations to treat different types of diseases including microbial infection and protozoan diseases. A previous study revealed that the crude extract of Myanmar medicinal plants showed *in vitro* inhibitory activity against *T. evansi*.¹⁾ The crude extract of *Vitis repes* Wight & Arn., *Phyllanthus simplex* Retz., *Vitex arborea* Desf., and *Ampelopsis brevipedunculata* Var. *heterophylla* showed antitrypanosomal activity against *T. evansi* with IC₅₀ values of 8.6 µg/mL, 96.1 µg/mL, 48.6 µg/mL, and 16.4 µg/mL, respectively. The isolation and structural elucidation of active ingredients in these plants were performed in this study.

Antitrypanosomal compounds from Myanmar medicinal plants

Bioassay guided investigation of extracts of the rhizome barks of *V. repens* Wight & Arn. led to the isolation of three antitrypanosomal compounds, resveratrol (**1**), 11-*O*-acetyl-bergenin (**2**), and

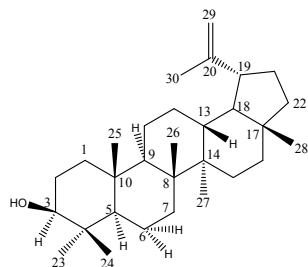
stigmast-4-en-3-one (**3**) with IC₅₀ values of 31.4 µg/mL, 61.2 µg/mL, and 62.8 µg/mL, respectively.²⁾ The attempt obtaining the active ingredients of *P. simplex* Retz. led to the isolation of two compounds, lupeol (**4**) and Ψ-taraxasterone (**5**) with IC₅₀ values of 98.4 µg/mL and 115.4 µg/mL, respectively. According to bioassay-guided fractionation, hopenyl-3β-*O*-palmitate (**6**) with IC₅₀ value of 68.2 µg/mL was isolated from the leaves of *V. arborea* Desf. The fruits of *A. brevipedunculata* led to the isolation of β-amyrin palmitate (**7**) with IC₅₀ value of 60.8 µg/mL and resveratrol (**8**). The isolated compounds (**1-7**) exhibited mild to moderate antitrypanosomal activity against *T. evansi*. Among of the isolated compounds, resveratrol (**1**) has best activity against *T. evansi*. It is likely that the isolated compounds (**1-7**) might be good leads for development of trypanocidal drugs. In conclusion, medicinal plants used in Myanmar may offer a potential use to prevent and treat disease caused by *T. evansi*.



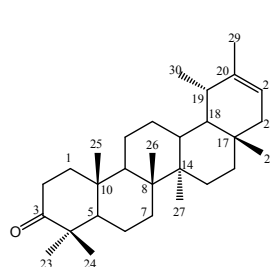
1, 8 (*trans*-resveratrol)

2 (11-*O*-acetyl bergenin)

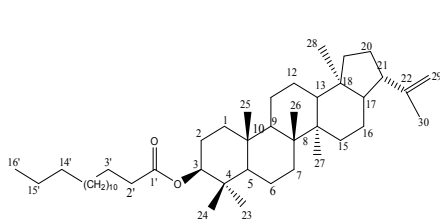
3 (stigmast-4-en-3-one)



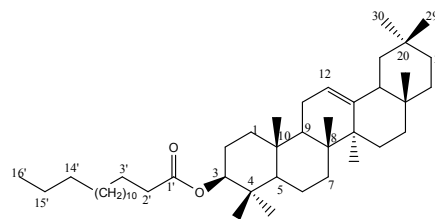
4 (lupeol)



5 (Ψ-taraxasterone)



6 (hopenyl-3β-*O*- palmitate)



7 (β-amyrin palmitate)

¹⁾ Bawm, et al., 2010. Evaluation of Myanmar medicinal plants for their *in vitro* antitrypanosomal and cytotoxic activities. *Journal of Veterinary Medical Science*, 72, 525-528.

²⁾ Khine, et al., 2012. Isolation of antitrypanosomal compounds from *Vitis repens*, a medicinal plant of Myanmar. *Natural Product Communications*, 7, 609-610.