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INFORMATION LETTER

IN VITRO ANTILEISHMANIAL ACTIVITY OF THE MEDICINAL PLANT *MACLURA AURANTIACA*

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ABSTRACT

Infections due to protozoa of the genus of Leishmania are responsible for a significant burden of disease, especially in the developing countries. Furthermore, the incidence of leishmaniasis continues to rise due to lack of a vaccine. Drugs commonly used for the treatment of the disease show varying levels of effectiveness and also have associated side effects. There is therefore, a need to develop newer drug therapies. The aim of our study was to assess antiprotozoal activity of the filtrate from hot extract, mother liquor from hot extract and filtrate from cold extract, mother liquor from cold extract of crude phenolics from Maclura aurantiaca growing in Kazakhstan.

Data reveal that Maclura aurantiaca contains active compounds, which could serve as an alternative agent in the control of leishmaniasis. Further studies would therefore be needed to determine its in vivo clinical response and associated toxicities.

KEYWORDS: *Maclura aurantiaca, Leishmania, total phenolic extract, medicinal plant.*

INTRODUCTION

Natural products are not only the basis for traditional or ethnic medicine. Only recently, they have provided highly successful new drugs such as Artemisinin. Furthermore, screening natural products found in all sorts of environments such as the deep sea, rain forests and hot springs, and produced by all sorts of organisms ranging from bacteria, fungi and plants to protozoa, sponges and invertebrates, is a highly competitive field where all of the major pharmaceutical companies are encountered. Already, many new natural product groups have revealed antiparasitic properties of surprising efficacy and selectivity, as will be shown in this review for plant-derived alkaloids, terpenes and phenolics. Many novel lead structures, however, have severe chemico-physical drawbacks such as poor solubility. Here, innovative drug formulations and carrier systems might help, as discussed by the authors in another article of this series. [*Kayser O et al., 2003*].

Each natural product has identification number (NPID) set by the National Center for Natural Products Research, USA.

Maclura aurantiaca (L.) Gaud. (Moraceae) is known to produce *several secondary metabolites* belonging to different chemical classes including prenylated flavonoids, which were found to have potent pharmacological effects. However, *Maclura aurantiaca* growing in Kazakhstan has not been sufficiently studied phytochemically or biologically. In this study we report the isolation, characterization and biological activity of 5 primary results from the fruits of *Maclura aurantiaca* growing in Kazakhstan.

The effectiveness of the plant's five fractions against L. donovani leishmaniasis strain at the dosage of 80 µg/ml showed results from 0% to 96.5%

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TABLE 1.

Primary antileishmanial action of filtrate from *Maclura aurantiaca* fruit hot extract.

NPID	129464
Sample Name	Filtrate from hot extract
Sample Code	YK1
Investigator(s)	Ross S.A.,Orazbekov Y.K.
Specimen part	Fruit
Geographic Location	Kazakhstan
Sample Type	Extract
Collaborator	Kazakhstan
Antileishmanial Inhibition Data in %	
Percent of Inhibition	94.4
Test Concentration	80 µg/mL

TABLE 2.

Primary antileishmanial action of filtrate from *Maclura aurantiaca* fruit cold extract.

NPID	129465
Sample Name	Filtrate from cold eextract
Sample Code	YK2
Investigator(s)	Ross S.A.,Orazbekov Y.K.
Specimen part	Fruit
Geographic Location	Kazakhstan
Sample Type	Extract
Collaborator	Kazakhstan
Antileishmanial Inhibition Data in %	
Percent of Inhibition	99.5
Test Concentration	80 µg/mL

TABLE 3.

Primary antileishmanial action of filtrate from *Maclura aurantiaca* fruit mother liquor from cold extract.

NPID	129466
Sample Name	Filtrate from mother liquor cold extract
Sample Code	YK3
Investigator(s)	Ross S.A.,Orazbekov Y.K.
Specimen part	Fruit
Geographic Location	Kazakhstan
Sample Type	Extract
Collaborator	Kazakhstan
Antileishmanial Inhibition Data in %	
Percent of Inhibition	43.2
Test Concentration	80 µg/mL

TABLE 4.

Primary antileishmanial action of filtrate from *Maclura aurantiaca* fruit mother liquor from hot extract.

NPID	129467
Sample Name	Filtrate from mother liquor hot extract
Sample Code	YK4
Investigator(s)	Ross S.A.,Orazbekov Y.K.
Specimen part	Fruit
Geographic Location	Kazakhstan
Sample Type	Extract
Collaborator	Kazakhstan
Antileishmanial Inhibition Data in %	
Percent of Inhibition	97.9
Test Concentration	80 µg/mL

TABLE 5.

Primary antileishmanial action of *Maclura aurantiaca* fruit crude extract.

NPID	129468
Sample Name	Crude extract
Sample Code	YK5
Investigator(s)	Ross S.A.,Orazbekov Y.K.
Specimen part	Fruit
Geographic Location	Kazakhstan
Sample Type	Extract
Collaborator	Kazakhstan
Antileishmanial Inhibition Data in %	
Percent of Inhibition	0.0
Test Concentration	80 µg/mL

(Tables 1-5).

The reservoirs of the disease are rodents, dogs and other wild animals. The disease is transmitted by mosquitoes of the genera *Lutzomyia* or *Phlebotomus*. Leishmaniasis is a major public health problem especially in the developing countries. According to the World Health Organization (WHO), the population of 88 countries is threatened by leishmaniasis and about 350 million people are at risk for the disease. The prevalence of leishmaniasis is 12 million with a rate of 2 million cases annually [*Modabber F, 1993*]. The clinical manifestations of leishmaniasis are recognized to be in three forms: visceral leishmaniasis or Kala-azar (VL), cutaneous leishmaniasis (CL) and mucocutaneous leishmaniasis (MCL) [*Desjeux P,*

2004]. CL the commonest form of leishmaniasis is endemic in Iran, Saudi Arabia, Syria, Afghanistan, Pakistan and in some South American countries [*Kassi M et al., 2008*]. More than 90% of the visceral leishmaniasis (VL) cases are recorded in India, Bangladesh, Indonesia and Sudan [*Kolodziej H, Kiderlen AF, 2005*]. According to WHO, almost 80% of the world's population turn to traditional medicine for their health care [*Avijit D et al., 2007*].

Animal to animal non-vector transmission of Leishmania major was investigated in Balb/c mice, a strain known for its susceptibility to this parasite. Both overt and unapparent infection (documented by positive spleen cultures) was possible after prolonged contact with infected animals. Similarly transmission of infection from infected mothers to their offspring was documented [*Nuwayri-Salti N, Khansa HF, 1985*].

EXPERIMENTAL SECTION

Plant material: Fresh fruits of *Maclura aurantiaca (L.)* (4 *kg*) were purchased in Shymkent, Kazakhstan, October, 2013

Extraction: Hot extract filtrate, mother liquor from hot extract, filtrate from cold extract, mother liquor from cold extract and crude phenolic extract from *Maclura aurantiaca* were studied. The method is being patented by innovation patent for invention and shall not be disclosed.

Antileishmanial assay

The antileishmanial activity of all analogues was evaluated in vitro against *Leishmania donovani* promastigotes by Alamar Blue assay [*Harrison JH, Jollow DJ, 1987; Mikus J, Steverding D, 2000*]. Alamar Blue assay is a colorimetric method used to detect cytotoxicity in drugs against Leishmania with Alamar blue dye. The activity is reported in terms of primary research with the test concentration of 80 µg*/ml*. Pentamidine and Amphotericin B are used as standards.

CONCLUSION

The colorimetry technique-based *in vitro* study of antileishmanial action of *Maclura aurantiaca* hot and cold extracts and mother liquor from hot and cold extracts demonstrated high inhibiting efficiency in comparison with the crude extract without such efficiency.

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REFERENCES

1. *Avijit D, Goutam M, Chitra M., et al.* In vitro antileishmanial activity of Aloe vera leaf exudate: A potential herbal therapy in leishmaniasis. Glycoconj J. 2007;24:81-86.
2. *Desjeux P*. Leishmaniasis: Current situation and new perspectives. Comp. Immunol Microbiol Infect Dis. 2004;27:305-308.
3. *Harrison JH, Jollow DJ*. Contribution of aniline metabolites to aniline-induced methemoglobinemia. Mol Pharmacol. 1987;32:423-431.
4. *Kassi M, Kassi M, Afghan AK., et al.* Marring leishmaniasis: the stigmatization and the impact of cutaneous leishmaniasis in Pakistan and Afghanistan. PLoS Negl Trop Dis. 2008;2(10):e259.
5. *Kayser O, Kiderlen AF, Croft SL*. Natural products as antiparasitic drugs. Parasitol Res. 2003 Jun;90:S55-62.
6. *Kolodziej H, Kiderlen AF*. Antileishmanial activity and immune modulatory effects of tannins and related compounds on Leishmania parasitized RAW 264.7 cells. Phytochem. 2005;66:2056-2071.
7. *Mikus J, Steverding D*. A simple colorimetric method to screen drug cytotoxicity against Leishmania using the dye Alamar Blue. Parasitol Int. 2000;48:265-269.
8. *Modabber F*. Chagas'disease, In: Tropical Disease Research, World Health Organisation, Genev, Ninth Programme Report of the UNDP/ World Bank/WHO. 1993.
9. *Nuwayri-Salti N, Khansa HF*. Direct non-insect-vector transmission of Leishmania parasites in mice. Int J Parasitol. 1985;15(5):497-500.