American-Eurasian Journal of Sustainable Agriculture, 3(2): 185-194, 2009 ISSN 1995-0748

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ORIGINAL ARTICLES

The Potential Uses of Melia Azedarach L. as Pesticidal and Medicinal Plant, Review

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Adnan Y. AL-Rubae, The Potential Uses of *Melia Azedarach* L. as Pesticidal and Medicinal Plant, Review, *Am.-Eurasian J. Sustain. Agric.*, 3(2): 185-194, 2009

ABSTRACT

Melia azedarach L. (Family: Meliaceae) is a deciduous tree that is native to northeastern India. It has several common names such as, White cedar, Persian lilac, Tulip cedar and Chinaberry. The plant has been introduced into several countries in Asia, North America and Latin America. In Jordan it has been planted as an ornamental plant for unrecorded number of years.

For the Indian natives it has been known for quite long time, that the tree members of family Meliacea are good source of folk medications. This fact drew the attentions of many scientists around the world to study the potential contribution of those plants to their efforts in finding a suitable, effective and environment friendly products to control pests and or diseases.

Extracts of fruits, seeds, leaves of *M. azedarach* have shown many characteristics of medicinal and pesticidal activities against several pathogenic and pest organisms respectively. In medical and veterinary entomological investigations, extracts of *M. azedarach* showed efficacy against the tick *Boophilus micoplus*, the malarial vector *Anopheles stephensi*, the dengue vector, *Aedes aegypti* and the human lice *Pediculus humanus capitis*. Insecticidal, acricidal, fungicidal and rodenticidal potentials of extracts made from various parts of the plant have been proven by many workers in several countries. The effect of *M. azedarach* extracts on the activity of NADPH-cytochrome c reductase and the cholinesterase in insects was also investigated.

Antiviral, antibacterial and antifungal potentials of the plant extracts have been reported by many investigators, working on human and animal diseases. A mong these diseases are skin Cellulitis and herpes simplex.

Key words: Melia azedarach, Anifeedant, Biopesticide, Limonoids.

Introduction

Plant species have been exploited for the treatment of disease by different ethnic societies in different parts of the world. According to the world heath organization (WHO) infectious disease are the number one cause of death world wide and account for 50 % of the death in tropical countries. It has revealed that about 80 % of individual from developing countries use traditional medicine, therefore such plant species should be investigated in order to have a better understanding of their pharmacological properties, efficacy and safety.

Insecticides of plant origin have been well known for decades. Many commercial products have been marketed world wide and have proved to be effective, efficient and less harmful to the man and his environmental components.

Melia azedarach commonly known as bread tree has been investigated extensively by many workers in reference to its potential activity as a pesticidal and medicinal plant.

This paper is a comprehensive literature review of the potentiality of using M. azedarach for pesticidal and medicinal purposes.

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Scientific name

Melia Azedarach Linn.

Family; Meliaceae

Derivation: Melia, Greek name of Manna Ash, refering to the resemblance of the leaves to those of the Ash, (Northern hemisphere Ash, genus Fraxinus); Azedarach from Persian azad = noble, and darach = tree.

Common names

This plant has possessed many local names according to the country where it is established. Among these names are:

Chinaberry, Persian lilac, pride of India, china tree, Indian lilac and breed tree (English; Bakain, Drek, Pejri, Padric (India); Bakainu (Nepal); Thamga (Burma); Inia (Hawai); Alelaila (Peurto Rice); Jacino (Panama); Aleli (Venzulea); West Indian Lilak, Lilac (West Indies); Lilas (Haiti, French); Cinnamumo (Brazili) and Zanzalacht(Jordan).

Standard trade name: White Cedar (WC)

Habitat and Description

A small to medium deciduous tree attaining a height of 5-15 m and a stem diameter of 110 cm. An attractive ornamental and shade tree with a high lateral branching. Hardy and drought resistant. Ferny foliage turning yellow in Autumn. Leaves are dark green on the upper surface and paler underneath. They emit a Punfent smell when crushed. Flowers are purple and fragrant. Fruits or berries are yellow, nearly round, smooth and so hard as a stone, containing 4 to 5 black seeds.

Distribution

Melia azedarach Linn. is native to tropical Asia. It is wide spread and naturalized in most of the tropics and subtropical countries. It was introduced and naturalized in Philippines, United States of America, Brazil, Argentine, many African countries and many Arab countries.

Pesticidal Potentials

A-Insecticidal, Acaricidal and Rodenticidal Activities

The Meliaceae plant family is known to contain a variety of compounds, which show insecticidal, antifeedant, growth regulating and development modifying properties (Nugroho *et al.* 1999; Nakatani et. al., 2004). Effects of M.azedarch extracts of various parts of the plant on many pests have been already reported (Saxena *et al.*, 1984; Schmidt *et al.*, 1988, Carpinella *et al.*, 2003; Nathan, and Saehoon, 2005).

An extensive work conducted by Wondscheer, j. and coworkers (2004) on larvicidal action of M. azedarach against the dengue mosquito A. aegypti in Brazil. Results showed the Potentiality of (MA) in controlling this insect via its larval stage.

In parallel manner to previous mentioned investigation(s), the larvicidial and oviposition detterent effects of fruit and leaf extracts from *M. azedarach* on *Aedes aegypti* (Diptera: Culicidae) were investigated (Carolina *et al*, 2004). A comparison tests of kernels of ripe fruits from *M. azedarach* and *A.indica* against larvae of dengue fever vector were carried out. The overall results indicated the superiority of *A. indica* over *M. azedarach* in insecticidal activity, but the LC(s) of the former fall within the confidence interval of the latter.

More work on the same vector A. aegypti was conducted by various investigators (Omena 2007). The newest research work by Coria, C. et al. (2008) proved that ethanolic leaf extract of M. azedarach is a strong larvicide on A. aegypti, and all tested larvae died before pupation, and significantly delayed development time, in addition to its inhibition ability of oviposition by the vector females. In comparison with leaf extract the fruit extract showed much weaker effects.

The efficacy of leaves and seeds methanolic extracts against the malarial vector *Anopheles stephensi* under laboratory conditions (Nathan *et al.*2006). This cooperative work of two groups, one from India and the other one from South Korea, proved that both extracts showed strong larvicidal, pupicidal, adulticidal, antiovipositional activity and biting deterrency, though seed extract exerted higher bioactivity than leaves extract at all doses tested. In their conclusion investigator expressed optimism regarding the potentiality of *M. azedarach* in controlling the insect effectively and less expensively than available chemical pesticides, yet call for the need to study the mode of action of the biopesticide under field condition.

Many triterpenoids present in plants of the Meliaceae family are described as showing insectiaidal activity. Bohnenstengal et al. (1999) reported the isolation of three meliacarpin derivatives from M. azedrach leaves. The activity of meliacarpin derivatives were tested on larvae of the polyphagous pest insect Spodoptera littoralis by incorporating it into artificial diet to larvae in a chronic feeding bioassay. Results indicated a comparable insecticidal activity to the well known lipopesticide azadarachtin found in neem tree. The crude ethanolic seed extract of Bazilian M. azedarach showed both phagoinhibitory and anti-molting activities to the hemophagous insect Rhodnius prolixus, one of the vectors of chagas disease (Kelecom et al., 1996).

The efficacy of ripe fruit extracts of *M. azedarach* L. was evaluated against the tick *Boophilus microplus* (Acari: Ixodidae). Organic solvent extracts were prepared and tested on larvae and engorged females by immersion. Hexane-Chloroform extracts of ripe fruit showed good efficacy on larvae mortality, and to less level of efficacy in case of female adults (Borges *et al.*, 2003). The investigation came up with a conclusion implying that crude extract of *M. azedarach* fruits was as effective as azadirachtin of neem tree in inhibiting the oviposition and embryogenesis of *B. microplus* as it has been observed by some investigators (Williams 1993; Mansingh & Williams 1998).

The other interesting observation stated by Borges *et al.* (2003) is that most of the fruit extract activity was seen in the a polar and intermediate polarity solvents which could be attributed to components structurally related to steroids and terpenoids.

In the phytochemistry analysis of *M. azedarach* ethanol extracts, it revealed the presence of triterpenoids and steroids, respectively, and both seeds and leaves also presented alkaloids and condensed tannis. These compounds are able to inhibit development or insect feeding and also they display ovicidal activity in insects (Mulla and Su, 1999).

An interesting research paper in medical entomology dealt with control measure of the head louse, *Pediculus humanus - capitis* using *M. azedarach* extracts (Carpinella *et al*, 2007). Pediculicidal and ovicidal activity of the extract and oil from fruits were tested by filter paper bioassay. The chemical analysis of the ethanolic extract revealed the presence of flavonoids and triterpenes. The authors indicated that one triterpene which they, then, named Meliartenin with an isomer 12-hydroxyamoorastatin, is the most effective biopesticide. Its spectra and mode of action are similar to the well known limonoid compound azadirachtin (Carpinella *et al.*, 2003)

The effect of fruit extract from *M. azedarach* on juvenile hormone titer and protein content in the hemolymph of two species of noctuid lepidopteran larvae was investigated (Schmidt *et al.* 1998) which indicated a promising future for *M. azedarach* fruit extract as a good stomach poison insecticide for the studied insects. This work was based on a review by Ascher *et al.* (1995) on the source of unique natural products in integrated pest management (IPM), medicine, industry and other purpose, and also on work of several investigators (Breuer *et al.* 1998; Lee *et al.* 1991; Schmidt *et al.* 1997).

Several investigators have concentrated on constituents of *M. azedarach* as a feasible biopesticide against plant sap sucking insects such as aphids and whitefly (Abou-Fakhr *et al.*, 2001; Abou-Fakhr *et al.* 2000a - 2000b; Palectosetal 1993; Kraus *et al.* 1987). Fruit and leaf aqueous and methanolic extracts have shown comparable effects against adult whiteflies. This finding has nominated *M. azedarach* to be a potential source for management of the sweet poato whitefly *Bamisia tabaci*.

The inhibition activity of NADPH - Cytochrome reductase and Cholinesterase in *Spodopter frugiberda* larvae by *M. azedarach* extracts was investigated (Breuer, *et al.*, 2003). Their finding indicated that consumption of extract containing diet resulted in a 31 % inhibition of the Cholinesterase activity.

Comparison of the insecticidal efficacy of chinaberry, endol and pepper tree against the maize stalk borer, Busseola fuscal_(fuller) (Gebre & Azerefegne 1999) showed that M. azedarach extract was effective in reducing the number of larvae. Leaves (either fresh or dried) were similar in their activity. Although it has proved that chinaberry is most active plant against the pest, the investigators suggested that more than two applications of extracts would be necessary to reduce the pest numbers significantly.

Several studies were performed using M. azedarach extracts against economical insects mostly lepidopterous (Hellpap $et\ al.$, (1994). The effects of methanolic extracts of neem and chinaberry seeds on the oviposition behavior and hatchability of eggs of $Erias\ vitella$ were investigated under laboratory conditions (Gajmer et el 2001). There was no eggs laying when the female moths were fed on a sucrose diet containing 6, 8 & 10 % chinaberry and neem extracts.

It was stated by some investigators that even closely related pest species can differ markedly in susceptibility to the same plant extract or pure allelochemical (Isman 1993; Akhtar & Isman 2004 a,b). Accordingly a comparative bioactivity of selected extracts from meliaceae members and some commercial insecticides against two noctuid caterpillars, *Trichopusia ni* and *Psedaletia unipunctata* were conducted (Akhtar et al., 2006). Among Meliaceae members tested was M. azedarach (Syn. M. toosendan in China). Its seed

extract proved to be the most active antifeedant against *P. unipunctata* than *T. ni*. This plant contains limonoids closely related to what is found in neem tree, *Azadirachta indica*. Some of the limonoids isolated from the fruits of chinaberry are melianol (Lavie and Jain 1967), meliacin, meliacarpin (Lee *et al.* 1991) and meliartenin (Fig 1-C) (Carpinella *et al* 2002).

Meliantiol showed strong antifeedant properties against the desert locust, S. gregaria (Kraus et al 1981), and meliartenin (Fig 1-A) inhibited larval feeding of E. panuelate and S. eridania (Carpinella et al 2002). Seed oil of M. azedarach acted as a strong oviposition deterrent for rice gall midge, Orseolia oryzae, and a feeding deterrent for oriental army warm, Mythimna separata (Chiu et al.1984). Fruit extracts of both M. azedarach and A. azadirachta showed feeding deterrent effect against the larvae of Plutella xylostella at higher doses (Charleston et al., 2005) and also against a variety of insect species belonging to three orders including Coleoptera, Lepidoptera and Orthoptera (Carpinella et al 2003). Seed oil sprays were also effective against citrus red mite, Panonychus citri and the orange spiny white fly, Aleurocanthus spiniferus but was not harmful to several predatory mites such as Amblyseius spp.(Chiu 1989).

The rodenticidal potentiality of both neem and chinaberry trees was investigated. Seed extracts of both plants proved to be effective in inhibiting folliculogenosis in albino rats (Roop et al 2005). Polar extract (MeOH) and non polar extract (Hexane) were used in this investigation. The results revealed the significant activity of both extracts from both plants in reducing the number of normal single - layered follicles in rat. This preliminary experiment could lead to further studies in order to find a suitable rodenticide which is ecologically safe and biologically active.

Reports on using flowers of *M. azedarach* (Pandey *et al.* 1995) and flowers and leaves (Khalil *et al.*1979) as abortifacient in East A fica and Saudia Arabia have been recorded. In rats, 50 % ethanolic extract of stem bark of the same plant was found to be devoid of anti - implantation activity (Bhakuni et al.,1969).

More recent report on utilizing leave extract of *M. azedarach* (MA) showed that it is inactive as a pregnancy interceptive (Keshri *et al.*,2003) On the other hand it was found that chloroform extract of (MA) roots showed a significant contraceptive activity.

The antifertility of extracts from (MA) and ferula assafoetida was investigated by measuring changes in activities of key enzymes of carbohydrate metabolism in rat uterus on day 7 of pregnancy (Keshri et al 2004). It was observed that on the day 7 of pregnancy one key enzyme of glycolytic pathway (Phosphofructokinase) was significantly reduced in the uteri of treated rats as compared to controls. Hexosemonophosphate pathway also appeared to be sensitive to treatment with the plant extracts and showed an inhibitory effect on the enzyme activities of glucose -6-phosphate dehydrogenase. Oxidative energy metabolism through TCA cycle was maximally affected by the treatment. Investigators concluded that plants lacking phytoestrogens may intercept pregnancy by their ability to disrupt energy metabolism in rat uterus during implantation, especially the oxidative pathway.

B - Fungicidal Potential

The activity of ethanolic leaf, seed and fruit extracts from (MA) in controlling plant and human pathogenic fungi such as Aspergillus flavus, Fusarium monitiform, Microsporum canis and Candida albicans has been reported (Carpinella et al, 1999).

In other study, a serial agar dilution method was utilized in proving the fungistatic activity of hexanic and ethanolic extracts from fruit, seed kernels, and leaves of (MA) against A. flavus, Diaporthe phaseolorum var. meraidionales, Fusarium oxysporum, F. solani, F. vertllioides, and Schlerotina sclerotiorum. Three compounds were isolated from crude extracts and identified as, vanillin (Fig 1-B), hydroxyl -3- methoxcinnamaldehyde and (+-) pinoresinol (Carpinella et al 2003). In a subsequent research effort, the seeds of ripe fruits from M. azedarach L.were utilized to isolate the active compound Scopoletin (Fig 1-C), a hydroxyl coumaramin (Carpinella et al 2005), and the subsequent testing of its antifungal synergestic effect. Results revealed a good antifungal activity of the isolated compounds when tested against F. verticilloides as well as its synergistic effect when it was combined with two conventional fungicides mancozab or carboxin. A summary of various pesticidal activities along with pests targeted, plant parts utilized and basic related references is shown in Table 1.

The antibacterial potential of *M. azedarach* L. was tested using crude leaf extracts against human pathogenic bacterial strains (Abdul Viqar *et al* 2008). Various bacterial pathogenic were subjected to extracts (using Petrol, Benzene, Ethyl acetate, Methanol, Aqueous, Chloramphenicol). The bacterial strains were *Basillus subtilis*, *Proteus mirabilis*, *Shigella flexeneri*, *Sh. dysenteriae*, *Plesiomonas shigellides*, and *Staphylococcus aureus*. Ethyl acetate was the most effective extract followed by methanolic fraction that inhibits the growth of all tested pathogens.

Fig. 1: Chemical structures of Limonoid compounds extracted from *Melia azedarach*, A- meliartenin, B- vanillin, C-scopoletin

Table 1	Daatiaidal	Dotomticlity	of 11	4J
Table 1:	: Pesticidal	Potentiality	of M .	Azedarach L

Pesticidal Activities	Targeted Pests	Extracts	Basic References
Larvicida & Anti oviposition	Aedes aegypti	L, F	Carolina et al, 2008, , Carolina et al. 2004,
			Coria et al 2008, Correges 1994, Omena 2007
			Wondscheer, et a.l., 2004
Larvicidal, Pubicidal, Anti oviposition,	Anopheles stephensi	S	Nathan, et al 2006
Biting deterrency			
Larvicidal	Spodoptera littoralis	L	Bohnensstengel et al, 1999.
Phagoinhobitory, Antimolting	Rhodinis prolixus	Seeds	Kelecom et al., 1996
Larvicidal Anti oviposition, anti	Boophilus microplus	F	Borges et al, 2003, Williams 1993, Mansingh
embryogenesis			& Williams 1998
Pediculicidal&Ovicidal	Pediculus humanus capitis	F	Caprinella et al, 2003-2007
Biopesticidal	Bamisia tabaci	F, L	Abou-Fakhr et al, 2001, 2000a-b, Falectos
			et al, 1993, Kraus et al 1987
Anticholinesterase	Spodoptera frugiperda	F	Breuer et al, 2003
Larvicidal	Busseola fuscala	S, L	Gebre& Azerfegne, 1999
Anti oviposition, Anti hatchability	Erias vitella	S	Gajmer et al, 2001
Antifeedant	Pseudaletia unipunctata	S	Akhtar et al 2008
	Trachiaplusia ni	S	
	Spodoptera eridania	F	Carpinella et al., 2002
Anti oviposition Anti feedant	Orseolia oryzae	S	Chiu et al., 1984
	Mythimna separata	S	
Anti feeding	Plutella xylostells	F	Charlestone et al 2005
Biopesticidal	Panonychus citri	S	Chiu, 1989
	Aleurocanthus spiniferus	S	
Rodenticidal	Albino rat	S	Roop et al 2005,
		L	Keshri et al 2003, Keshri et al, 2004
Fungicidal	Aspergillus flavus,	S	Carpinella et al, 1999-2003-2005
	fusarium monitiform,		
	Microsporum cans		
	Diaporthe phseolorum		
	Schlertina sclertiorum		

F= Fruit, L= Leaf, S= Seed Medicinal Potentials

MA flower extracts was prepared and used to treat bacterial skin diseases in children (Saleem et al. 2008) (Fig 2,3). The methanolic extract of flowers was used to make a cream preparation. An activity comparison of the prepared cream and the skin drug, neomycin was made. The diameter of infected area (mm²) before and after the two weeks treatment. The results showed that (MA) cream was a significantly potent cure in several cases. (MA) flowers extract showed its potential in curing rabbits suffering from a skin infection produced by Staphylococcus aureus. The healing effects were found comparable to the known drug neomycin (Saleem et al., 2002).

Meliacine, a peptide isolated from leaves of *M. azedarach* inhibited the multiplication of foot and mouth disease virus (Wachsman et at.1998). It also exhibited an antiviral activity against herpes simplex virus when aqueous extract of chinaberry was made and examined on *Vesicular stomatitis* (VSV), polio and herpes simplex

(HSV) viruses in cell cultures (Wachsman et al. 1982). The purified extracts from leaves of (MA) which contains meliacaprin inhibited VSV and HSVI multiplication in vitro when added after infection with no cytotoxic effect (Alche et al. 2002).



Fig. 2: Patient suffering from cellulitis on chin and surrounding areas. (a) Before treatment, (b) after treatment of 7 days, (c) after treatment of 15 days.

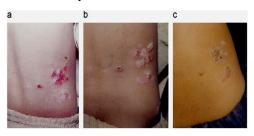


Fig. 3: Patient suffering from secondary bacterial infection on lateral side of the back. (a) Before treatment, (b) after treatment of 7 days, (c) after treatment of 15 days.

Balbc / mice inoculated with ocular herpes simplex virus type-1 (HSV-1) was treated with meliacine by topical administration 3 times a day for 3 consectetive days. *M. azedarach* extract significantly reduced the incidence (Pifarre *et al* 2002). Histological examination of corneas from (MA) treated animals revealed no tissue damage.

M. azedarach extracts was viable in reducing the viability of Trichmonas vaginalis (Lee et al. 2007). The plant extract has an anti protozoal effects on T. vaginalis cells through the inhibition of cell multiplication as well as the impairment of protein synthesis.

An in vivo study was conducted in rats to demonstrate the effect of aqueous extract of (MA) on ethylene glycol - induced Nephrolithiasis (Christina et al. 2006). The investigators were able to show that (MA) extract reduced the urinary calcium, oxalate and phosphate levels. Thus (MA) has inhibitory potential on induced nephrolithiasis judged by serum and urine levels of creatinine.

Some active ingredients present in the lipid fraction of (MA) extracts were experimented on rats under Gipsing - restrain stress to induce ulcers.

(Moursi et al. 1984). The finding indicated that lipid component of (MA) which is mainly phytosterol fraction was capable to reduce the free and total HCl combined with reduction of total acidity, and significant increase of the volume of gastric juice, thus revealing its antiulcer potentiality.

In the field of veterinary medicine, the larvicidal and ovicidal activity of (MA) extracts on the helminthus *Haemonchus contortus* (Maciel *et al.* 2006) was reported. Both leaves and seed extracts revealed the presence of triterpenoids and steroids, and both also presented alkaloids and condensed tannins. Compounds present in leaves are different from these in seeds, since the former inhibit mainly egg hatching and the later, larval development.

An in vitro tests of (MA) extract activity against *H. contortu* were conducted by (Akhtar *et al* 2000), as a preliminary studies. The plant extracts were directly placed in contact with eggs or larvae of the parasite to evaluate the effect on egg hatching and larval development. Results proved that these extracts were effective as anti egg hatching and also as an inhibitor of larval development. Summarization of medicinal potentiality of *M. azedarach* against organisms or diseases is shown in Table (2).

Conclusion

There has been a growing concern by governmental organizations as well as the public in general over increasing number of chemicals produced and used for medicinal, agricultural and industrial purposes. The main concern is centered upon the human being wellbeing and his environmental safety. Accordingly there has been

a continuous efforts to find a suitable, effective and environment friendly materials to substitute the most dangerous synthetic chemicals. Plant materials are becoming increasingly important as a source of medicinal and pesticidal components, although folk practices in utilizing plant materials for medicinal purposes as well as materials used to deter economical pests have been recognized for centuries.

Table 2: Medicinal Potential of M. Azedarach

Medicinal activities	Organism or Disease	Extracts	Basic Reference(s)
Antibacterial	Proteus mirabilis	L	Abdul Viqar et al., 2008
	Shigella flexeneri,		
	Plesimonas shigellidis		
	Staphyloccocus aureus		
	Bacillus subtilis		
Antiviral	Foot and mouth Disease,	L	Wachsman et al., 2008
	Herpes simplex,(VSV),	L	Wachsman et al., 1982
	(HSV)(VSV), (HSV1)	L	Alche, L. et al. 2002
	Ocular Herpes simplex, (HSV1)	L	Pifarri, et al. 2002
Antiprotozoal	Trichomonas vaginalis	S,L	Lee et al., 2007
Antinephrolihiasis	Ethylene glycol-Induced Nephrolthiasis	L,S	Christina, et al., 2006
Antiulcer	Stomach ulcer in rats	L,S	Oursi, et al., 1984
Anti helminthal	Haemonchus contortus	L,S	Maciel, et al, 2006
			Akhtar, et al., 200

L= Leaf, F= Fruit, S = Seed

In this review we made an effort to compile information on pesticidal and medicinal activities of the chinaberry *Melia azedarzch*. Survey of literature revealed the presence of many lemonoids compounds such us mliacaprin, scopoletin, meliartenin in addition to other groups of compounds. Extracts of seeds, leaves, fruits are most parts of the plant which they were used in most investigations. Various literature indicated successful attempts of scientists to prove the potentiality of this plant in combating pests such as malarial mosquito, dengue mosquito, lice and ticks under laboratory conditions. Activities of various extracts were proved to be effective against many economical pests including insects, mites, fungi and rodents.

Medicinal potential of *M. azedarch* against many pathogenic organisms including bacteria, viruses and parasites was reported via many investigations. Its activity to control some physiological illnesses such as induced stomach ulcer and ethylene- glycol induced nephrolithiasis was also recorded.

Although good scientists in many countries have been optimistic about the potentiality of *M. azedara ch* as a promising biopesticide to be incorporated into IPM programs, more work is required to upgrade the extraction and chemical analysis processes. Field application is, also, necessary to support laboratory experiments and also to enable scientists making a concrete decision of the component effectiveness. Investigations of the safety of extracted materials towards man and the environment components is needed in days ahead.

Acknowledgment

The author would like to express his gratitude to the International Institute of Education (IIE)-SRF, NY, USA for granting him one of their scholarships.

Appreciation is, also, extended to the Jordan University of Science and Technology (JUST) for offering a residency during the author's sabbatical leave, and for partial financial support.

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