



Anti-cancer, anti-inflammatory and anti-microbial activities of plant extracts used against hematological tumors in traditional medicine of Jordan

Areej M. Assaf^{a,*}, Randa N. Haddadin^a, Nedhal A. Aldouri^b, Reem Alabbassi^a, Sundus Mashallah^a, Mohammad Mohammad^a, Yasser Bustanji^a

^a Faculty of Pharmacy, The University of Jordan, Amman, Jordan

^b Faculty of Pharmacy, Philadelphia University, Amman, Jordan

ARTICLE INFO

Article history:

Received 1 August 2012

Received in revised form

22 November 2012

Accepted 26 November 2012

Available online 11 December 2012

Keywords:

Anti-cancer

Anti-microbial

Anti-inflammatory

Traditional medicine

Jordan

Hematological tumors

ABSTRACT

Ethnopharmacological relevance: *Mercurialis annua* L., *Bongardia chrysogonum* L., and *Viscum cruciatum* Sieb have been traditionally used by local herbalists in Jordan for the treatment of hematopoietic neoplasms.

Aim of the study: To determine the anti-cancer, anti-inflammatory and anti-microbial potentials of the three extracts against two of the most common hematopoietic malignancies in the Jordanian populations; Burkitt's lymphoma and Multiple myeloma.

Materials and methods: The anti-cancer activity was tested against the two cell lines (BJAB Burkitt's lymphoma and U266 multiple myeloma) using the MTT and trypan blue assays. The agar dilution assay was used to study the anti-microbial activity against Gram-positive bacteria, Gram-negative bacteria, anaerobic bacteria and yeast. The pro-inflammatory cytokines interleukin (IL) -1 β , IL-8 and tumor necrosis factor- α (TNF- α) were measured in the pretreated cell lines using ELISA assay to determine the anti-inflammatory activity of *Viscum cruciatum* Sieb against the two cell lines.

Results: The results show no evidence of stimulation of tumor growth by any of the three extracts comprising cell lines from hematological malignancies, but *Viscum cruciatum* Sieb showed a selective anticancer activity against BJAB cells, with IC_{50} value of 14.21 μ g/ml. The antimicrobial effect was only noticed with *Viscum cruciatum* extract by inhibiting *Staphylococcus aureus*, *Candida albicans* and *Propionibacterium acne*, but not *Pseudomonas aeruginosa* at MIC of 1.25, 1.25, 0.625 and < 5 mg/ml, respectively. The highest activity was against the anaerobic bacteria *Propionibacterium acne*. *Viscum cruciatum* Sieb extract showed an inhibitory effect on the pro-inflammatory cytokine IL-8, but it increased TNF- α and IL-1 β secretions in BJAB cells. Whereas, it had an inhibitory effect on TNF- α and IL-1 β cytokines while it enhanced IL-8 secretions in U266 cells.

Conclusion: Among the three tested herbal extracts used in the traditional medicine in Jordan, only *Viscum cruciatum* Sieb showed high anti-cancer and anti-microbial potentials. They also had an anti-inflammatory effect. These observations raise the prospects of using *Viscum cruciatum* Sieb for treatment of diseases associated with some bacterial and fungal infections, for imbalanced cytokine production and for enhancing cancer and other immunotherapies.

© 2012 Elsevier Ireland Ltd. All rights reserved.

1. Introduction

Cancer is one of the major causes of death worldwide where the number of cancer patients is in continuous rise. A very recent study conducted worldwide showed that one in every six cases of cancer is caused by infections (de Martel et al., 2012). This fraction is even higher in less developed countries.

Application of methods to prevent and/or treat infection, such as the use of antimicrobial treatments, could have an effect on

future burden of cancer worldwide. Although antibiotics decreased the spread and severity of a wide variety of infectious diseases, bacteria and fungi have developed numerous mechanisms to escape old and new antimicrobial agents due to their uncontrolled use (Cowan, 1999). In this concern, the proper treatment of cancer and microbial infections would have a great impact on the population's health. This has drawn the attention and interest of researchers worldwide.

In Jordan, cancer is the second most frequent cause of death after heart disease where hematopoietic neoplasms (lymphomas and leukemias) are the most common malignancies (Jordan Cancer Registry Ministry of Health Report, 2010). Breast cancer was found to be the first cause of cancer in Jordan (C50 total 19.6%)

* Corresponding author. Tel.: +962 6 5355000x23363; fax: +962 6 5339649.

E-mail addresses: areej_assaf@ju.edu.jo, areej_assaf@hotmail.com (A.M. Assaf).

according to cancer mortality data in the year 2009. Lymphoma (total 8.1%) ranked third among all newly diagnosed cancer cases where Non-Hodgkin lymphoma accounted for 61.8% of all cases of lymphoma. The most common type of Non-Hodgkin lymphoma (NHL) in Jordan is Burkitt's lymphoma which represent the largest group (55%) of the childhood NHLs (10-years of age or younger) (Almasri et al., 2004). The same study also showed that leukemia were the most common cancer among Jordanians below 15 years of age accounting for 36%, followed by Lymphoma (27%) of all childhood cancers.

Due to the increasing cost of conventional treatments for cancer and the antimicrobial resistance for some antibiotics, this has encouraged people in different countries to depend more on folk medicine (Wood-Sheldon et al., 1997). Various medicinal plants have been used all over the world in daily life to treat different diseases. In developing countries and Jordan in particular, the use of medicinal plants in traditional medicine is very common where a large portion of the population relies on it for health care and particularly in the treatment of cancer.

Recent records reported that 80% of the people living in rural areas use medicinal herbs as primary healthcare system (Sakarkar and Deshmukh, 2011). The practitioners and herbalists in Jordan indicated that more than 150 plant herbs are still in use as traditional source of herbal medicine (Abu-Irmaileh and Afifi, 2003). Some of these herbs are used in traditional medicine for the treatment of cancer, mainly for Leukemia. Medicinal plants serve as therapeutic alternative and a safe choice which might reduce the high systemic toxicity and drug resistance indicated in chemotherapy that might limit the successful outcomes in most cancer cases. However, little is known about the possible medicinal application of these plants or their cytotoxicity (Mahasneh and El-Oqlah, 1999; Al-Hussaini and Mahasneh, 2009). From this concern and in recent years, medicinal plants have been gaining interest in the scientific community in Jordan, and more specifically, regarding cancer treatment.

The present study was conducted to screen and evaluate the anti-cancer, anti-inflammatory and anti-microbial potentials of extracts from three medicinal plants (*Mercurialis annua* L., *Bongardia chrysogonum* L. and *Viscum cruciatum* Sieb) that grow in Jordan where the traditional local herbalist uses them for the treatment of hematopoietic neoplasms (lymphomas and leukemias). These plants were selected depending on the information gathered from traditional healers and reputed informants and been reported to be within the flora of Jordan (Karim and Quraan, 1986; Karim and Quraan, 1988; Al-Qura'n, 2005).

To examine the three Jordanian medicinal plants' anti-cancer (anti-proliferation) and anti-inflammatory activities, they were tested against two of the most common hematopoietic malignancies in the Jordanian population; Burkitt's lymphoma (BJAB) and Multiple myeloma (U266) cell lines. The *in vitro* cytotoxic activity was measured using MTT assay for the determination of the anti-proliferative activity whereas their effect on the levels of the pro-inflammatory cytokines (TNF- α , IL-8, and IL-1 β) was measured using ELISA assay. To evaluate and determine the lowest concentrations of these plants that have an anti-microbial activity and inhibit the visible growth of the bacteria, minimal inhibitory concentration (MIC) assay was used. Up to our

knowledge, this is the first study to screen for their anti-cancer, anti-inflammatory and anti-microbial potentials in hematopoietic malignancies.

2. Materials and methods

2.1. Plant material

Plants were bought from traditional herbalists in Amman, Jordan. The taxonomic identity of each plant was authenticated by Dr. Nedhal AlDouri (Faculty of Pharmacy, Philadelphia University, Amman, Jordan) and voucher specimens were deposited there (Table 1).

2.2. Plant extraction

The plant samples (leaves of *Mercurialis annua* L., tuber of *Bongardia chrysogonum* L. and leaves of *Viscum cruciatum* Sieb) were dried carefully under shade at room temperature and then homogenized to fine powder and stored in airtight bottles. Suitable amounts of the powdered plant materials were soaked in methanol (20 g/l) for five days at 37 °C with continuous shaking (Labtech, Korea). The crude methanolic extract was filtered using 125 mm filter paper (Albet, EEC) and then the solvent was evaporated to dryness under reduced pressure using rotary evaporator (Heidolph laborota, Germany). The residues were further subjected to dryness by incubating them for 8 days at 37 °C. The powdered crude extracts were either used directly or stored in an air-tight container for further use.

2.3. Cell lines and culture conditions

BJAB (Burkitt's lymphoma) and U266 -IgE producing myeloma (Multiple myeloma) cell lines were kind gifts from Dr. M.J Browning (University of Leicester, UK). Cells were cultured in RPMI 1640 ready mix with L-Glutamine (PAA Laboratories, Austria) supplemented with 10% heat inactivated fetal bovine serum (FBS) (PAA Laboratories, Austria), Gentamicin (50 μ g/ml), penicillin (100 U/ml), and streptomycin sulfate (100 mg/ml) (Sigma) and incubated in a humidified atmosphere of 5% CO₂ at 37 °C.

2.4. Anti-cancer activity

2.4.1. Herbal extract activation dose and time course

To determine the activation dose and time course, 1×10^5 cells/ml were either left untreated (culture in growth medium alone) or stimulated with 200, 100, 150, 100, 50, 25, 12.5, 6.25 μ g/ml with the three plant extracts separately in growth medium for variable times (24, 48 and 72 h). Cell viability as indicated in the following session was assessed and the dose and time course was determined depending on the experimental read-out.

2.4.2. Cell viability analysis

Cell numbers and viability were assessed every 24 h for three days using trypan blue (Sigma) dye exclusion. The dye exclusion test is based on the concept that viable cells do not take up trypan

Table 1
List of the studied plants.

Plant extract	Part used	Family	Herbarium specimen code	plant uses in traditional medicine
<i>Mercurialis annua</i> L. (Hasheshat alzeabak)	Leaves	Euphorbiaceae	1 EUP-NA	Leukemia
<i>Bongardia chrysogonum</i> L. (Uruf-el-Deek)	Tuber	Berberidaceae	1 BER-NA	Different types of cancer including lymphoid cancers.
<i>Viscum cruciatum</i> Sieb (Red-berry mistletoe)	Leaves	Loranthaceae	1 LOR-NA	Different types of cancer including lymphoid cancers.

Download English Version:

<https://daneshyari.com/en/article/5837830>

Download Persian Version:

<https://daneshyari.com/article/5837830>

[Daneshyari.com](https://daneshyari.com)