Full Length Research Paper

Palliative treatment of cancer in resource poor settings: Traditional medicine perspective

Florence Dushimemaria¹ and Davis R. Mumbengegwi²

¹Science, Technology and Innovation Division, Multi-disciplinary Research center, University of Namibia, Private Bag 13301, 340 Mandume Ndemufayo Avenue, Pionier spark, Windhoek, Namibia.
²Science, Technology and Innovation Division, Multi-disciplinary Research center, University of Namibia, Private Bag 13301, 340 Mandume Ndemufayo Avenue, Pionier spark, Windhoek, Namibia.

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This study aimed to determine the suitability of ethnomedicinal plants as a suitable option for palliative care of cancer in Namibia. To achieve this, key informant interviews were conducted in central and northern parts of Namibia on the use of ethnomedicinal plant products for palliation of cancer. Information from surveys on the medicinal use of plants in Oshikoto and Zambezi regions of Namibia for ailments such as tumors were used to select plants for phytochemical analysis. Plants were collected and extracts were prepared for analysis for phytochemical detection using thin layer chromatography, anti-protease, antioxidant and phytochemical quantification of Colophospermum mopane and Shinziophyton rautanenii plants. Findings from key informant interviews revealed pain management for cancer patients was the primary form of disease management at health care facilities in contrast to an established holistic palliative care system. As a result, patients looked towards alternative treatment from ethnomedicinal plant sources in their bid to palliate cancer and seek hope. Phytochemical analysis of indigenous plants collected, revealed the presence of class compounds such as flavonoids, alkaloids, triterpenes, coumarins and anthraquinones as well as biological activities such as anti-protease, antioxidant properties. In conclusion, phytochemical properties of the six plants were consistent with their ethnomedicinal use, making them a suitable option for treatment of cancer in resource poor settings such as Namibia. Further studies are required to evaluate safety and mode of action.

Key words: Palliative care, Namibia, medicinal plants, anti-cancer.

INTRODUCTION

Non-communicable diseases (NCD) such as cancer, diabetes, cardiovascular disease, as well as Human immunodeficiency virus infection and acquired immune deficiency syndrome (HIV/AIDS) and chronic respiratory disease were responsible for over 63% of the fifty seven million mortalities that occurred in 2008 (WHO, 2011). The World Health Organization (2011) report on NCD, shows that over 85% of premature deaths from NCD occurred in low-middle income countries. In Namibia, 19% of deaths were due to cardiovascular diseases while cancer, chronic respiratory disease and diabetes contributed 3% each respectively. The incidence of cancer...
in Namibia is on the rise. Kaposi sarcoma and prostate cancers are the leading cancers among the male population while breasts and cervical cancer are more common in females (Namibian Cancer Registry, 2011). Between 2006 and 2009, the frequencies were 22.1 and 19.2%, respectively, while statistics (Namibian Cancer Registry, 2009) showed a lower proportion of 19.2 and 12%, for Kaposi sarcoma and prostate cancer in males respectively. During the period of 2006 to 2009 (Namibian Cancer Registry, 2011), the most prevalent cancers in women were breast cancer (27.6%) and cervical cancer (17.1%). During the previous reporting period (Namibian Cancer Registry, 2009), a total of 4,949 cancer cases were recorded in comparison to 6,464 total cases between the period of 2006 to 2009 (Namibian Cancer Registry, 2011). These numbers reflect that cancer is a public health concern in Namibia, and hence emphasize the necessity of care and support for individuals with life-limiting conditions (Webster et al., 2007; Thomson, 2012).

Despite the evolution of treatment options of cancer such as chemotherapy, radiotherapy, surgery, hormonal treatment or a combination of these, effective and affordable cancer treatment is still illusive for many individuals. Factors such as disease progression, type of cancer, cost of treatment, lack of cancer management professionals and resources all hamper effective cancer treatment and management. In Namibia, a patient has to go through a long period of referrals before accessing proper treatment. First report is at a local clinic, from which patient is sent to a district hospital, followed by regional district, where one can consult with an oncologist; a patient may need to be referred to the central hospital in Windhoek before effective treatment and monitoring is initiated. By the time an opportunity for effective treatment is available, prognosis is often very poor and treatment options are expensive and beyond the reach of 56% of the Namibian population who live in rural resource poor settings.

Palliative care is a multi-dimensional, multi-disciplinary approach to treatment, which focuses on alleviating symptoms and distress arising from treatment serious disease and its treatments (Powell et al., 2010), for both the patient and their relatives (WHO, 2011). The African Palliative Care Association (APCA) of Namibia, in conjunction with partners such as the Cancer Association of Namibia, the Ministry of health and social services, United States Agency for International Development (USAID), Catholic AIDS Action (CAA) and Hospices of Hope, strive to increase awareness for the need for palliative care as well as access. Despite these efforts, access to effective palliative care is still illusive in Namibia (Palliative care training ends in capital, 2014). The APCA further advocates to avail morphine in order to effectively manage suffering of patients. Options for addressing chronic pain in palliative care involve use of opioids such as morphine (Webster et al., 2007). In resource poor settings, poverty makes it hard to access effective palliative treatment (Harding, 2008). In addition to this, legislative policies are not in place, especially when it comes to inclusion of alternative therapy options such as traditional medicines, further hampering effective palliative care (Webster et al., 2007; Powell et al., 2011; Logie and Harding, 2005).

Traditionally, plants have been a vital resource of medicines for health care provision (Thomson, 2010; Malwii-Nyiirenda and Malwiichi, 2010), yet there is a renewed interest in research towards the discovery and development of plant-derived medicines for mainstream usage as, many medicines in clinical use owe their origin to plants (Thomson, 2010). In addition, Sharma et al. (2011) observed increased reliance on traditional medicine evident in developing countries as a primary healthcare provision. Medicinal plants owe their chemotherapeutic properties to the presence of bioactive constituents such as alkaloids, terpenes and particularly polyphenols, which are known for antioxidant plus anti-inflammatory qualities (Farombi and Owoeye, 2011). For instance, Bernard and Alayinka (2010) reported pharmacological effects that cucurbitacins, a triterpenoid steroid conjugate possess analgesic, anti-inflammatory, antioxidant and antiproliferative activities. The antioxidant properties of plant derived medicines are capable of palliative, curative and preventative pharmacological effects for chronic disease such as cancer (Thomson, 2010). Traditional medicine has two goals: to cure disease and thereby prolong life or provide comfort and relief, therefore making disease easier to live with (Mudigonda and Mudigonda, 2010; Powell et al., 2011).

In this study, the potential usage of Namibian indigenous plants for palliative care in a resource poor setting, with emphasis on cancer and other non-communicable diseases, is discussed. Furthermore, key informant interviews were conducted. Chemical profiles of plants used as baseline data for characterization and validation of plants’ usage in traditional settings.

MATERIALS AND METHODS

Key informant interviews

The Key informants (KI) interviews were conducted with practitioners in cancer treatment and care in the Khomas and Oshana regions of Namibia on the incidences of cancer in Namibia. Five key informants (referred to as KI1, KI2, KI3, KI4 and KI5) were interviewed on the use of alternative medicines in treatment of cancer within cancer patients in Namibia.

Plant species reviewed

Plants with an ethnomedical background were obtained using literature search (Watt and Breyer-Brandwijk, 1962; Palgrave, 1981; von Koenen, 2001; Cheilkyoussef et al., 2011a; Cheilkyoussef et al., 2011b), and based on responses obtained in a survey conducted in the Zambezi region of Namibia (Du Preez et al.,
Further search revealed little or no evidence of proven medicinal evidence of plants. Plant material was sustainably harvested from the Zambezi region of Namibia, using guidelines from the National Botanical Research Institute (NBRI). Voucher specimens were prepared and sent for authentication at the NBRI as different ethnic names can refer to the same plant or different names to the same plant. Confirmation of scientific names can lead to proper identification of collected plants.

**Preparation of bioactive extracts**

Harvested plant material was cut into small pieces and dried at room temperature for two weeks before being ground to a fine powder. The ground plant material was then used to prepare organic plant extracts using methanol as solvent and sterilized distilled water to prepare aqueous extracts. After soaking ground plant for 7 days, mixture was filtered and solvent was evaporated. This was followed by dry freezing to totally remove solvent, resulting in dry crude extracts of various plant parts, such as leaf, root, twig and bark.

**Chemical profile investigation**

Plants were screened for known anti-cancer properties using chemical assays such as anti-protease activity, antioxidant activity and selected phytochemical compounds. Firstly, the antioxidant and anti-protease activity of the different plant extracts was investigated using 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulphonic acid) (ABTS) and radiograph film with gelatin respectively. Methanolic portions of different plant parts were screened for various selected phytochemical compounds, such as flavonoids, alkaloids, triterpenoids, coumarins and anthraquinones, according to Harborne (1998). Table 1 shows the various solvent systems and chromogenic reagent used to detect the listed phytochemicals using thin layer chromatography.

**Phytochemical quantification**

Plant material from Colophospermum mopane and Shinziophyton rautanenii were analyzed for the total content of saponins, alkaloids and phenols. Total saponin and alkaloid was quantified using methods adapted from Edeoga et al. (2005) to determine percentage yield. Total phenolic content was analyzed using a method contained in Jing et al. (2010) with slight modifications, and gallic acid was used to develop a calibration curve in order to expresses phenolic content as gallic acid equivalents (GAE) µg/ml. Antioxidant activity was investigated using a method adopted from Jing et al. (2010) and Re et al. (1999). A standard graph developed from ascorbic acid was used to estimate the antioxidant activity. Each phytochemical was quantified in triplicate from each sample.

**RESULTS**

Collected plants were identified (Table 2) using local names within the community and their identity was validated scientifically by the NBRI. The validation of plant names, by scientific means affords universal comparison of the same plant, even if it’s from different communities.

Chemical profiling of the plants revealed the presence of different phytochemicals. High anti-protease and antioxidant activity was detected in all plant parts, with the exemption of Acanthosicyos naudinianus shoots, which contained no detectable anti-protease activity. Different phytochemicals such as ascorcin, anthraquinone, alkaloids, flavonoids and triterpenoids were detected and were observed to be distributed in different tissues of the plants (Table 3). This development implies that the local community members may sustainably utilize plant material with the assurance that either plant parts contain potentially therapeutic phytochemicals.

Furthermore, based on literature review (Watt and Breyer-Brandwijk, 1962; Palgrave, 1981; von Koenen, 2001; Cheikhhoussen et al., 2011; Cheikhhoussen et al., 2011), responses on the use of medicinal traditional plants and phytochemical profiles of the six collected plants (Table 2), two plants; S. rautanenii and C. mopane root and bark extracts were analyzed for the total content of alkaloids, saponins, phenols and antioxidant activity (Figure 1). Both the roots of S. rautanenii (9.64±4.6% yield) and C. mopane (11.13±2.7% yield) displayed the highest alkaloid content while the bark extract of S. rautanenii (2.08±0.5% yield) had the lowest alkaloid content. Meanwhile, the C. mopane root (205.4±9.3 GAE µg/ml) had the highest phenol content and the C. mopane bark (12.6±1.7 GAE µg/ml) extract had the lowest phenolic content. Saponin quantification revealed that the bark of S. rautanenii (13.6±10.4%) was the highest saponin content while the root extract of S. rautanenii (1.8±0.7%) was the lowest saponin yield. The S. rautanenii root (945.6±231.1 AAE µg/ml) and bark (226.7±17.6 AAE µg/ml) extracts had the highest and lowest antioxidant activity, respectively.

**DISCUSSION**

Namibia has a wealth of traditional practices, which includes substantial ethnomedicine knowledge. This is passed on from a traditional knowledge holder to younger members of the community. Sadly, this does not happen in all instances, which leads to loss of traditional heritage. Namibia needs to take advantage of its current wealth of information, to properly document and validate Namibia’s heritage. This will increase awareness of traditional based medicines in the country and potentially lead to inclusion of traditional plant based therapies in mainstream medicine.

In Namibia, some individuals suffer from cancer experience chronic pain, which is partly associated with the disease and also as a result of side effects from cancer treatments. Such pain makes living with cancer difficult and can be unbearable in advanced stages of cancer. In Namibia, since many patients present very late (K11) progressive cases, at which time pain levels need to be managed to bearable levels, the availability of affordable pain relieving medications is vital. In Namibia, morphine is the medication of choice for individuals experiencing excruciating pain, in cancer patients or...
**Table 1.** Solvent systems and chromogenic reagents for thin layer chromatography.

<table>
<thead>
<tr>
<th>Phytochemical</th>
<th>Solvent system</th>
<th>Chromogenic solvent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alkaloid</td>
<td>Ammonium hydroxide: Methanol, 3:200</td>
<td>Dragendorff reagent</td>
</tr>
<tr>
<td>Anthraquinone</td>
<td>Ethyl acetate: Methanol:Water, 100:17:13</td>
<td>10% KOH in methanol</td>
</tr>
<tr>
<td>Triterpenoid</td>
<td>Hexane:Ethyl acetate, 17:3</td>
<td>Liebermann burchard reagent</td>
</tr>
<tr>
<td>Coumarin</td>
<td>Chloroform</td>
<td>10% KOH in methanol</td>
</tr>
<tr>
<td>Flavonoid</td>
<td>Butanol:Aceticacid:Water, 4:1:5</td>
<td>1% Aluminium chloride in methanol</td>
</tr>
</tbody>
</table>

**Table 2.** Medicinal plants collected for the study, their reputed use, local names and voucher specimen numbers deposited with NBRI.

<table>
<thead>
<tr>
<th>Scientific name</th>
<th>Local name</th>
<th>Family</th>
<th>Traditional use</th>
<th>Voucher specimen #</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. rautanenii</td>
<td>Mankettii</td>
<td>Euphorbiaceae</td>
<td>Sores on body surface</td>
<td>FD03</td>
</tr>
<tr>
<td>C. mopane</td>
<td>Omusati</td>
<td>Fabaceae</td>
<td>Swollen testis</td>
<td>FD02</td>
</tr>
<tr>
<td>Capparis tomentosa</td>
<td>Mudyangwe</td>
<td>Capparaceae</td>
<td>Poison, wound healing and anti-inflammatory</td>
<td>FD08</td>
</tr>
<tr>
<td>Lessertia benguellensis</td>
<td>Ndendeoma</td>
<td>Fabaceae</td>
<td>Syphilis, bloody urine and tonsils</td>
<td>FD06</td>
</tr>
<tr>
<td>Commiphora africana</td>
<td>Muwowo</td>
<td>Burseraceae</td>
<td>Abdominal cramps, anticancer and snake bite remedy</td>
<td>FD05</td>
</tr>
<tr>
<td>Acanthosicyos naudinianus</td>
<td>Muputwi</td>
<td>Curcubitateae</td>
<td>Poison, wound healing, edible and antiinflammatory</td>
<td>FD04</td>
</tr>
</tbody>
</table>

those suffering from other NCD, according to KI5. The APCA and Namibia’s Ministry of Health and Social Services are currently working on legislation which supports availability of morphine, even to the healthcare analyst I (MIA) levels in health care institutions (KI4).

However, the effectiveness of such a strategy relies hugely on the availability of such drugs. With lacking supporting legislation (Logie and Harding, 2005) coupled with lack of monetary funds in poor resource settings, palliative care is often unattainable. According to KI1, many cancer sufferers already seek assistance from traditional healers within the Namibian setting. KI2 and KI3 however presented a contradicting picture regarding the level to which individuals seek health care from elsewhere. According to KI1, mangosteen juice, Ativan (Lorazepam) and SOLAL are among natural products in use by cancer patients in Namibia. Mangosteen juice is derived from a fruit of *Garcinia mangostana*, a tropical tree, growing in Asian countries. Numerous studies have been conducted on the chemical properties of the “Queen of fruits”. These studies reveal compounds such as many variations of xanthones (Towatana et al., 2010). Its physiological properties include, high antioxidant activity, antitumor, anti-inflammatory, antiviral, antibacterial, anti-allergy properties but are not exclusive, (Pedraza-Chaverri et al., 2008). Use of combination treatments such as lorazepam, diphenhydramine plus metoclopramide and dexamethasone, to control vomiting and nausea as side effects arising from anticancer treatments are also common (Kris et al., 1987).

A source, (Olowokudejo et al., 2008) concedes that traditional medicine is a reliable source of effective, affordable and easily accessible therapeutic entities. However, it’s important to know that effective palliative care does not take the place of a prescribed treatment regimen. A look at these six Namibian plants (Table 2) revealed the presence of different bands of phytochemical compounds, using thin layer chromatography. Phytochemical compounds have been shown to confer anti-inflammatory (Bellik et al., 2013) and analgesic properties (Ojie et al., 2013), which are all beneficial to combat NCDs. Thin layer chromatography (TLC) results suggests that different kinds of triterpenoids and anthraquinones are present, as evidenced by the numerous bands observed on TLC plates (Table 3). It follows that, observed antioxidant activity may be due to the presence of phytochemicals (Table 3). In another study conducted in Botswana (Motlhanka, 2008), *C. mopane* methanolic extracts displayed radical scavenging activity. Antioxidant activity is commonly attributed to phenolic compounds, however, spearson correlation analysis revealed a correlation=0.58 (n-12, p=0.048) between alkaloid content and antioxidant activity. Plants from the euphorbiaceae family, such as S.
Table 3. Phytochemical profile of medicinal plants collected from the Zambezi region, Namibia.

<table>
<thead>
<tr>
<th>Plant sample</th>
<th>Anti-protease</th>
<th>anti-oxidant</th>
<th>Coumarin</th>
<th>Alkaloid</th>
<th>Flavonoid</th>
<th>Triterpene</th>
<th>Anthraquinone</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. rautanenii bark</td>
<td>+++</td>
<td>+++</td>
<td>++</td>
<td>+</td>
<td>+</td>
<td>+++</td>
<td>-</td>
</tr>
<tr>
<td>S. rautanenii root</td>
<td>+++</td>
<td>+++</td>
<td>+</td>
<td>+</td>
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<td>+++</td>
<td>+++</td>
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<tr>
<td>C. mopane bark</td>
<td>+++</td>
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<td>++</td>
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<tr>
<td>C. mopane root</td>
<td>+++</td>
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<td>++</td>
<td>+</td>
<td>+</td>
<td>+++</td>
<td>-</td>
</tr>
<tr>
<td>A. naudinianus shoot</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>A. naudinianus tuber</td>
<td>+++</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>C. africana twigs</td>
<td>+++</td>
<td>+++</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>C. africana roots</td>
<td>+++</td>
<td>+++</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>L. benguellensis leaf</td>
<td>+++</td>
<td>++</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td>C. tomentosa root</td>
<td>+++</td>
<td>+++</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>++</td>
<td>++</td>
</tr>
</tbody>
</table>

Key: ++++ = high, + = low, - = no detection.

Figure 1. Quantification of phytochemicals in the root and bark of C. mopane and S. rautanenii depicted as depicted in A) Alkaloids, B) Antioxidant activity, C) Phenolic content and D) Saponin.
have been found to confer antineoplastic activities (Soetan and Aiyelaagbe, 2009), antioxidant activity (Dasari et al., 2012) and this was attributed to the presence of phenolic acids. The phytochemical profile (Table 3) and quantification (Figure 1) suggests that the use of these plants in the traditional setting is rational and may be useful as an anticancer traditional alternative treatment (Wahab et al., 2010).

In the traditional setting, water is used as a solvent for preparation of medicinal treatments. However, organic solvents such as methanol, dichloromethane are used because they extract bioactive compounds more efficiently (Jo et al., 2011; Govindappa et al., 2011; Elkady, 2012). In addition to water, palm wine made from a tree, locally known as makalani palm (Hyphaene petersiana) is used to prepare medicinal portions, even though this method is rare. Therefore, with the wealth of opportunities presented by Namibia’s abundance of indigenous plants, there is a need for research into the safety and efficacy of plant derived extracts using in vitro assays to determine the anticancer effects of these plants. Further studies may also lead to standardization and dosage regimen of plant based supplements for use as alternative anticancer medicinal implements.

Conclusion
Cancer is an increasingly common cause of morbidity and mortality in Namibia. Providing healthcare to cancer patients in Namibia is a challenge not only because of the lack of treatment options, but also because of the lack of financial resources for treatment. This study shows the potential of medicinal plants to provide an option for palliative care of cancer patients. Further study of such medicinal plants may result in their becoming a mainstream as either a palliative treatment option or a potential cure for some early stage cancers in rural and even urban settings.

Conflicts of interest
The authors declare that they have no conflicts of interest.

ACKNOWLEDGEMENTS
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