EVALUATION OF A TOPICAL NATURAL PRODUCT FORMULATION WITH *CANTHARANTHUS ROSEA* AND *CYNODON DACTYLON* FOR THE TREATMENT OF SQUAMOUS CELL CARCINOMA IN A GELDING. A CASE STUDY

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ABSTRACT. A 20-year-old gelding suffering from 10 months of relapsing squamous cell carcinoma (SCC) on the penile sheath was treated with a natural remedy as surgical intervention was not successful. A daily application of herbal ointment healed the ulcer within 21 days. No relapse of ulcer was observed 3 months post heal.

Keywords: squamous cell carcinoma, natural product therapy

INTRODUCTION

The allopathic chemotherapy practices for tumour treatment in veterinary and medical treatment has been exposing patients to severe general systemic toxicity instead of selective cytotoxicity of cancer cells. Therefore, a natural product formulation according to *Siddha* practice was adopted to evaluate selected herbs known to be efficacious against tumour in human to be applied on a squamous cell carcinoma ulcer in a gelding .

Squamous cell carcinoma (SCC) refers to a malignant neoplasm of the epithelium line, the internal and external lining of the body, accounting to 80 to 90 percent of all cancers in the veterinary and medical field. Epithelial tissue is found throughout the body such as in the skin and lining of organs and internal passageways such as gastrointestinal tract.

Carcinomas are divided into two major subtypes. First type is adenocarcinoma which develops in an organ or gland which is capable of secretion. For example, the mammary gland that produces milk, and other organs such as colon, prostate and lung that secrets mucus. Another type is SCC which originates in the squamous epithelium.

MATERIALS AND METHODS

A gelding suffering from chronic SCC was diagnosed with tissue samples taken from an ulcerative and non-healing wound mass, and confirmed as SCC by laboratory diagnosis.

The gelding was subjected to a natural therapy after the failure of three surgeries to halt the remission at the same spot on the penile sheath. This was despite four intralesion injections of cisplatin, at one-week intervals to halt remission, as the SCC was resistant to the drug. Therefore, further surgical intervention was stopped,

as repeated anaesthesia of a senile horse is not recommended. A topical application that covers the entire SCC ulcer was carried out daily.

Selected herbs harvested locally was washed, cleaned, cut into small pieces and dried in a shed before it was crushed into smaller pieces. Among the important ones are *Catharanthus rosea* (Shohel *et al*., 2014; Kabesh *et al*., 2015 and Joyce *et al*., 2011) and *Cynodon dactylon* (Janani *et al*., 2011). The exact formula is not revealed for copyright purposes.

Catharanthus rosea known as *Nityakalyaani* in Tamil, a *Siddha* medicine, is an Indian origin herb. Its use in cancer treatment was long before chemical chemotherapeutics came into practice. The plant, apart from its anti-cancer activity, also has anti-bacterial activity (Kabesh *et al*., 2015) which may have contributed synergistically to the control of pus-forming bacteria, in the success of the SCC treatment.

Cynodon dactylon, also known as *Arugampul* in Tamil, has been used as a healing agent in *Siddha* medicine for thousands of years, mainly as a 'blood purifier'. 'Blood purification' is a very general term being claimed to purify a biological system, without specific site of action. Therefore, the herb awaits a scientific study to specify its action. A few compounds in this grass is known to have anti-cancer activities (Janani *et al*., 2011). These mixed herbs was then heated up with sesame oil to absorb active ingredients. The medicated oil was then bottled and applied on the ulcerating SCC for possible healing effects.

RESULTS

The progress in the healing SCC ulcer is illustrated in Figures 1 to 4.

The cost and efficacy of surgical and cisplatin injection for 4 weeks has failed to cease remission. Therefore, the cost and efficacy of the current natural therapy is compared to cisplatin treatment in Table 1.

DISCUSSION

The decision to initiate chemotherapy was difficult as the horse is senile and the side-effect may be severe with vincristine or cisplastin. The relapsing SCC has been completely cured without remission for 3 months post-healing. This result shows that, natural remedy could be applied topically

Table 1. Comparison of cost between chemotherapy and natural therapy for SCC treatment

SCC treatment for an adult gelding	Cisplatin treatment (Inter-lesion Injection)	Natural Therapy
Cost/week(RM)	150.00	50.00
Total cost for 4 weeks	600.00	200.00*
Drug Resistance	Present	Not present
Remarks		Healing achieved in 21 days and no remission for 3 months post healing till euthanasia.

* The cost if treatment continued for 4 weeks. The current natural therapy cured SCC in 3 weeks.

Figure 1. Suture breakdown. Post third surgery due to SCC remission. Topical application day 1.

Figure 2. Fifth day post application with marked granulation tissue invading the healing ulcer.

Figure 3. Thirteeenth day post application with marked ulcer reduction with wound shrinkage

Figure 4. Complete closure of SCC ulcer 20th day post application.

without any tissue and systemic toxicity without compromising the safety of a senile patient. This finding paves the way for the development of biopharmaceuticals from a natural product for veterinary and medical chemotherapy.

However, the current success on topical cancer treatment is limited as systemic malignancies could not be treated albeit metastasis in carcinomas are rare. Therefore, with extensive research and development, the bio-active compounds could be identified to formulate intramuscular or intravenous chemotherapeutic drugs. A biomolecular research is vital to identify the mechanism of action of each herbal extract and its compounds separately.

The ultimate aim of this study was to develop a natural anti-cancer compound by validating its effect on animals which then could be extrapolated for application on biotechnological research and development of biopharmaceuticals to cure mankind from dreaded malignancies. Cervical carcinoma (CC) is a type of SCC that affects women globally, resulting in death in severe cases (Priscilla *et al*., 2015). The current topical application could be used to validate an intracervical application on women detected with CC at its early stage without having to undergo toxic chemotherapy.

Certain alkaloids such as vincristine from the plant *Catharanthus rosea* has been proven to exert cytotoxic and anti-neoplastic activity in cell linings, *in vitro* as well as *in vivo* in animals and humans. However, the cytotoxicity of alkaloids are very severe, causing general systemic toxicity and should be administered intravenously by veterinary and medical professionals with caution. Conversely, the natural products in this study could be used without much side-effects and it was observed to be superior to cisplatin, whereby healing was achieved in just 21 days without recurrence and drug resistance.

The discovery of novel compounds has to undergo a lengthy procedure of etchical, safety and clinical trials before approval by authorities such as the US Food and Drug Administration (FDA) that may cost billions for approval of one anti-cancer or any other drug (Daniel and Norman, 2000). For example, thousands of chemically synthesised drugs are being tested for more than ten years. Thus, to eventually obtain only one drug approval by the FDA is not a viable effort.

This tedious scenario could be avoided by using natural products, by identifying evidence based efficacious ethnomedicine herbs which are subjected to direct bio-active compound extraction and identification. Therefore, tropical countries should formulate their own system of drug discovery and approval without the involvement of the FDA, thereby minimising the cost and time to unveil bio-active compounds of tropical herbage at a faster pace. As funding is always a constraint for ethical and safety procedures, government funding and favourable drug discovery policies has to be established.

Many scientific studies has been done to prove the efficacy of bio-active compounds (namely the secondary metabolites such as the alkaloids, terpenoids, flavanoids, saponins) and others as anti-neoplastic with other bio- activities (Simeon *et al*., 2015). However, the availability of

these compounds may vary in concentration according to environmental stresses. Therefore, bioinformatics has to be globally established to identify quality and high concentration yielding tropical herbages.

In conclusion, the medical and veterinary industry awaits a safer and more efficacious chemotherapy to alleviate the side-effects of chemically synthesised drugs and to minimise the cost of cancer treatment. The cost effectiveness of cancer treatments may extend the use of a drug in a wider range of animals, especially pets, saving them from euthanasia and chronic drug toxicity. The successful animal validation may pave the way for novel and safe drug discoveries for medical applications.

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