TheRole of Traditional Medicines as Chemopreventive and Suppressive Agents in Cancer Treatment Deanova Insiratu Nurul Andini¹, Gilang Kurniawan², Nahla Akila Fikria³

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Abstract

The purpose of this study was to determine the role of traditional medicine as a chemopreventive and suppressive agent in the treatment of Deanova Insiratu Cancer. This study is a qualitative study, this study will use a retrospective and prospective observational approach. Data will be collected from the medical records of patients who have used Deanova Insiratu previously, as well as from direct observation and interviews with individuals who are currently using or have experience with this traditional medicine. Research Results Cancer or malignant tumors can occur due to the growth of body tissue cells that proliferate abnormally. Cancer prevention can be done with healthy living habits and avoiding risk factors that can cause cancer. Cancer treatment can be done in 4 ways, namely by surgery, radiotherapy, immunotherapy and chemotherapy. Cancer screening can be done with mammography, ultrasonography (USG), and Magnetic Resonance Imaging (MRI). Natural ingredients that have effects as cancer prevention and help cancer treatment include Soursop leaves (Annona muricata), Celery leaves (Apium graveolans linn), Red Atai Spike leaves (Angiopteris ferox copel), Benalu Kepel (Dendrophthoe pentandra (L.) Miq.), and Tapak Dara leaves (Catharanthus roseus).

Keywords: Role of Traditional Medicine, Chemopreventive Agent, Suppository, Cancer Treatment Deanova Insiratu

1. INTRODUCTION

The incidence of cancer is increasing not only in developed countries, but also in developing countries with various types. Breast and cervical cancer are two types of cancer that have the highest frequency among other cancers that often affect women (Tjindarbumi and Mangunkusumo, 2002). Cancer is one of the diseases that causes a high mortality rate in Indonesia and in the world. Cancer is the uncontrolled growth and development of cells that occur in the body. The incidence of various types of cancer has increased in developing countries (Garcia et al., 2007).

Breast cancer and cervical cancer are the two most common types of cancer in women in Indonesia (Tjindarbumi & Mangunkusumo, 2002). The development of cancer is often found in advanced stages (metastatic) and involves complex molecular mechanisms that cause problems in its therapy (Gibbsb, 2000). Chemotherapy, which is one of the most possible treatments for advanced cancer, often fails due to the low selectivity of anticancer drugs.

Efforts to find anticancer drugs that are safe and selective for cancer treatment and prevention, especially those derived from medicinal plants, need to be carried out. Some anticancer drugs derived from plants have been used in cancer chemotherapy effectively. The alkaloids vincristine and vinblastine are examples of anticancer drugs that have long been used and their molecular mechanisms are known as well as taxol. Scientific theories on the molecular effects of anticancer medicinal plants on cancer cells are necessary for the development of safe and selective anticancer drugs (Cragg & Newman, 2005).

Cancer has become one of the significant health problems worldwide, with an everincreasing incidence rate and its detrimental impact on individuals and society. Although there have been advances in cancer diagnosis and treatment, conventional therapies are often expensive and can have serious side effects. Therefore, research continues to explore new strategies for cancer treatment that are more affordable, safe and effective. One area that is attracting attention is the use of traditional medicine as a chemopreventive and supportive agent in cancer treatment. Traditional medicine, with its diversity of natural ingredients and uses that have been known for centuries in various cultures, promises a potential source for further research in this context. However, although there has been a growing interest in the use of traditional medicine, there is still a significant lack of knowledge on the mechanism of action, effectiveness, and safety of many of these ingredients. Therefore, further research is needed to understand more deeply the potential of traditional medicines as chemopreventive and supportive agents in cancer management. In this context, this study aims to investigate the specific role of traditional medicine, with a focus on Deanova Insiratu, in the prevention and supportive treatment of cancer. Through a deeper understanding of the potential of these traditional medicines, it is hoped that we can develop a more holistic and integrated approach to cancer management, providing a wider range of affordable treatment options for individuals affected by cancer.

Previous research has shown that some of the natural ingredients used in Deanova Insiratu have antioxidant, anti-inflammatory, and anticancer activities. For example, certain herbs used in this traditional medicinal blend have been found to contain active compounds such as flavonoids, polyphenols, and terpenoids that have the potential to inhibit cancer cell growth, reduce inflammation, and boost the immune system. However, although the preliminary evidence is promising, there is still a lack of information that needs to be resolved. First of all, the exact mechanism of action of Deanova Insiratu in inhibiting cancer is still not fully understood. Further research is needed to reveal how the active compounds in this traditional medicine interact with the biological pathways involved in cancer development. In addition, it is also important to evaluate the effectiveness and safety of using Deanova Insiratu as a chemopreventive and supportive agent in cancer treatment. Well-controlled clinical studies need to be conducted to assess whether the use of this traditional medicine can reduce the risk of developing cancer in high-risk individuals, as well as whether it can help in improving response to conventional therapies and reducing side effects associated with cancer treatment. By deepening our understanding of the role of Deanova Insiratu and other traditional medicines in cancer management, it is hoped that we can develop a more holistic approach to the management of this disease, integrating conventional medicine and the effective and safe use of traditional medicines. In addition, it is important to consider the social, cultural and environmental context when discussing the role of traditional medicines such as Deanova Insiratu in cancer management. In many communities, the use of traditional medicine has been an integral part of health care practices for generations. This research should also take these factors into account to better understand how traditional medicine is integrated in the mindset and treatment practices of a particular community. A multidisciplinary and collaborative approach is essential in this research. Combining knowledge and expertise from fields such as pharmacology, chemistry, molecular biology, as well as traditional and complementary medicine, can help in better understanding the complexity of interactions between traditional medicines and body systems, and open up opportunities for the development of more effective and innovative therapies.

Public education also needs to be improved to remove the stigma and ignorance surrounding the use of traditional medicine in cancer treatment. Providing accurate and reliable information about the potential and limitations of traditional medicine, as well as promoting an open mindset towards evidence-based medicine, can assist individuals in making informed treatment decisions appropriate to their needs. As such, research into the role of traditional medicines such as Deanova Insiratu in cancer management is not just about exploring the therapeutic potential of natural materials, but also about understanding their cultural and social context, promoting interdisciplinary collaboration, and increasing people's understanding and awareness of the various treatment options available to them.

2. Methods

This is a qualitative study, which will use a retrospective and prospective observational approach. Data will be collected from the medical records of patients who have used Deanova Insiratu previously, as well as from direct observation and interviews with individuals who are currently using or have experience with this traditional medicine. Data Collection: Data will be collected through several methods, including: Analysis of patient medical records to obtain information on cancer diagnosis, cancer type and stage, conventional treatments that have been or are being used, as well as the use of Deanova Insiratu. In-person interviews with individuals using Deanova Insiratu to obtain information on dosage, frequency of consumption, duration of use, and changes in their health condition. Surveys or questionnaires to collect data on side effects experienced, perceptions of the effectiveness of this traditional medicine, and adherence to drug use.

Data Analysis: The data collected will be analyzed quantitatively and qualitatively. Statistical analysis will be used to compare the demographic and clinical characteristics between the groups that used Deanova Insiratu and those that did not. In addition, thematic analysis will be conducted to identify common patterns in the experience of using this traditional medicine, reported side effects, and perceptions of its benefits. Evaluation of Effectiveness and Safety: During data analysis, the effectiveness of Deanova Insiratu as a chemopreventive and supportive agent in cancer treatment will be evaluated based on changes in clinical parameters such as tumor size, disease progression rate, and quality of life. In addition, the safety of using this traditional medicine will be evaluated by monitoring reported side effects and possible complications. Exploration of Mechanism of Action: Although the study is primarily observational, efforts will be made to elucidate the mechanism of action of Deanova Insiratu in cancer prevention and treatment support. This may involve an in-depth literature review of the active compounds in this traditional medicine and their potential interactions with biological pathways involved in cancer. However, it should be noted that further research will be required to validate these findings experimentally.

3. **Results and Discussion**

Etiology of Cancer

Cancer or malignant tumors occur due to abnormal growth of body tissue cells, caused by neoplasia, dysplasia, and hyperplasia. Neoplasia is a condition of cells found in tissues that proliferate abnormally and invasively, dysplasia is a condition of cells that do not develop normally with an indication of changes in the nucleus (cell nucleus), hyperplasia is a condition of normal cells in the tissue experiencing excessive growth (Ariani, 2015). Cancer is a disease caused by abnormal growth of body tissue cells, developing rapidly, uncontrollably and continuing to divide (Indah, 2010). Cancer is a disease that can attack and arise due to abnormal growth of body tissue cells that turn into cancer cells in their development (Lubis, 2009).

The cause of cancer is that a healthy body is unable to defend itself against cancer, this occurs due to a complex interaction between exposure to carcinogens and mutations that have accumulated in several genes called oncogenes, thus activating cell division that affects embryonic development. Another cancer gene is the tumor suppressor gene, which stops cell division. Causes of acquired gene damage are: viruses, radition, environmental carcinogens as well as food and hormones. Other factors that influence the occurrence of cancer are age, nutritional status, hormonal balance and stress response (Kowalak, 2011).

Molecular Pathophysiology of Cancer

Abnormal cells form a group and begin to proliferate abnormally, letting growthregulating signals in the cell's surroundings. Cells gain invasive characteristics resulting in changes to the surrounding tissue. Cells infiltrate the tissue and gain access to lymph and blood vessels, which carry the cells to other areas of the body. This is called metastasis (cancer spreading to other parts of the body). Cancer cells are called malignant neoplasms and are classified and named after the tissue in which they grow. The failure of the immune system to destroy abnormal cells quickly and appropriately causes the cells to grow too large for normal immunity to handle. Specific categories of agents or factors that play a role in carcinomagenesis (malignant transformation) include viruses and bacteria, physical agents, chemical agents, genetic or familial factors, dietary factors, and hormonal agents. (Suddarth, 2016)

Cancer is characterized by uncontrolled growth and metastatic acquisition. In many cases, activation of oncogenes and/or deactivation of tumor suppressor genes leads to uncontrolled cell cycle progression and inactivation of apoptotic mechanisms. In malignant tumors there is a decrease in the tissue-specific affinity of cell-cell binding to receptors and an increase in the number of cell-moving receptors. Activation of membrane metalloproteases opens up metastatic physical pathways for the widening spread of cancer cells. Genetic changes that occur include mutations, chromosomal translocations and deletions, dysregulation of expression or activity of signaling pathways. Recent studies have suggested that epigenetic changes characterize cancer because they are cancer-promoting cells and initiators of carcinogenesis (Sarkar et al., 2013).

The process of carcinogenesis begins with the initiation stage of neoplasia where irreversible changes occur in somatic cells. Initiation occurs due to cell instability caused by exposure to carcinogens resulting in gene mutations and neoplastic formation. Activation of oncogenes plays an important role in neoplastic transformation, as mutations of tumor genes cause changes in cellular responses that refer to gene dysregulation in biochemical signal control pathways resulting in disruption of the natural processes of cell communication, development, and differentiation. Cells that undergo transformation will continue to divide accompanied by further mutations before the manifestation of malignant lesions (Devi, 2005).

The second stage of carcinogenesis is promotion where the transformed cells are stimulated to proliferate further until cellular imbalance appears. This stage requires transformation driven by long-term exposure to carcinogens. Third is progression, or commonly called pre-neoplastic cell conversion. Pre-neoplastic cells transform to the developmental stage of malignancy, followed by the accumulation of gene mutations and the extent of pre-neoplastic cell clones (Devi, 2005).

The fourth stage is tumor angiogenesis, tumor growth needs to be supported by growth factors and efficient removal of toxic molecules as well as adequate blood intake. These supporting factors are channeled by blood vessels, but the blood vessels in normal and tumor tissues are different. Tumor vessels are often dilated, saccular and tortuous and may also contain tumor cells in the endothelial lining of the vessel. Blood flow in tumors may be slower compared to adjacent normal tissues and tumor microvasculature may show hyperpermeability of plasma proteins. The fifth stage is tumor metastasis, as tumor progression continues, cells will detach from the tumor mass and invade nearby tissues. The detached cells will also enter the blood and lymph circulation so that they enter other tissues or organs and then expand. This causes distant metastases, resulting in widespread cancer (Devi, 2005).

Sukardja (2010) explains that cancer is a cell growth disease, which results from damage to genes that regulate cell growth and differentiation. This cell division is uncontrolled, the cells then invade and damage other biological tissues either by direct growth in adjacent tissues (invasion) or by cell migration to distant places. Carcinogenesis (the process of changing normal cells into abnormal ones beginning with damage called cancer).

Cancer is the process of excessive abnormal cell changes that result in damage to normal body tissues that will die. This can trigger cancer cells to continue to grow and never die. Sukardja (2010), explains that all cells, both normal and cancer cells, divide within a cell cycle. However, normal cells in the body are in balance between the speed of these cells to divide and form new cells with the speed of cell death.

Clinical Manifestations of Cancer

- a. Cancer cells spread from one organ or part of the body to another organ or part of the body through invasion and metastases so that the manifestation is according to the affected organ or body.
- b. Cancer causes anemia, weakness, weight loss (dysphagia (difficulty swallowing), anorexia, obstruction), and pain (often late stage).
- c. Symptoms are caused by destruction of tissue and replacement by nonfunctional cancerous tissue or highly productive tissue (e.g. bone marrow disorders and anemia or overproduction of adrenal steroids), pressure on surrounding structures, increased metabolic demands, and impaired production of blood cells (Suddarth, 2016).

Cancer Chemopreventive and Supportive Agents

Disease prevention behaviors through foods, additives, micronutrients and natural compounds are constantly being developed. This behavior is called chemoprevention and the substances used are called chemopreventive agents. Chemoprevention is the use of natural or synthesized agents that reverse, inhibit or prevent the development of cancer (Sharma, 2012).

The main goal of chemoprevention is to delay the occurrence of cancer and also reduce its incidence. Successful chemoprevention requires the use of agents capable of inhibiting specific molecular stages of the carcinogenesis pathway. Studies over the past four decades have shown that natural and synthetic chemopreventive agents are able to inhibit carcinogenesis through two main pathways: inhibition of carcinogen activation and induction of xenobiotic metabolizing enzymes, thereby protecting against environmental toxic effects. In addition, chemopreventive agents have molecular targets such as proteins involved in cell cycle progression and proliferation, anti-apoptotic proteins, drug transport; multi drug resistance (MDR); multi-drug resistance-related protein (MRP), growth factor pathway, NF-!B activation pathway, angiogenesis, inflammatory proteins such as COX2 (Sharma, 2012).

Chemopreventive targets not only focus on preventing cancer from occurring, but also inhibiting the stages of carcinogenesis as a whole. Chemopreventive agents generally have the activity of inhibiting cancer development and can increase the likelihood of cure and reduce the pain experienced by cancer patients. The reality that is often encountered is that people affected by cancer are not satisfied with just taking anticancer drugs (chemotherapy) given by doctors alone, but also still look for other alternatives from plants (herbs) that are believed to have anticancer properties. However, alternatives do not always guarantee to accelerate healing, it can also happen the other way around. Alternative herbs that are believed to be medicinal, actually reduce the potential of anticancer drugs in killing cancer cells. (Sharma, 2012).

Cancer Prevention

Most types of cancer can be prevented by healthy living habits from a young age and avoiding factors that cause cancer. Although the exact cause of cancer is not yet known, everyone can make efforts to prevent it by living a healthy life and avoiding the causes of cancer. We can do this by implementing CERDIK behavior:

- Regular health checks
- Get rid of cigarette smoke
- Physical activity
- Healthy diet with balanced calories
- Get enough rest

In addition to taking precautions, we can also confirm the condition of our body, whether there are cancer seeds or not by early detection. To prevent cervical cancer, the Visual Inspection with Acetic Acid (VIA) method is used. While for the early discovery of breast cancer is done by the detection method of clinical breast examination (Sadanis) and breast self-examination (Sadari) (Indriyati, 2017).

Medical Treatment of Cancer

There are four types of cancer treatment (Foye, 1996): surgery, radiotherapy, immunotherapy and chemotherapy.

1. Surgery

Surgery is one of the treatments for cancer. However, cancer treatment with surgery generally only works on cancer cells that have not metastasized. But if cancer cells have spread to other organs, surgery cannot be done.

2. Radiotherapy

Radiotherapy is the use of radioactivity to destroy tumor cells. The advantage of

radiotherapy cancer treatment is that it causes as little damage as possible to the surrounding normal tissues. Combined surgery and radiation therapy can be more beneficial because radiotherapy can destroy microscopic cancer cells that may remain after surgery. In addition, radiation can shrink large tumors, reduce local recurrence and may decrease the chance of metastasis. The types of radiation rays commonly used for cancer therapy are Gamma (γ) Rays of Cobalt-60 (Co-60) and X-rays. However, this radiation has a very dangerous side effect, namely the presence of X-rays that have low wavelengths and high energy can affect normal cells around the target cancer cells. This can damage and even kill normal cells.

3. Immunotherapy

Immunotherapy is a cancer treatment that utilizes the immune response in the patient's body to destroy cancer cells. Immunotherapy is an advanced treatment because it can delay the reappearance of cancer cells for a long period of time. BCF (Bacillus Calmette Guerin) as a weakened Mycrobacterium bovis bacterial derivative is an immunotherapy agent because it actively enhances the general immune response and stimulates macrophages. BCF is nonspecific as it does not utilize antigens unique to a particular type of cancer cell.

4. Chemotherapy

Chemotherapy is the treatment of cancer through the use of chemical agents (anticancer drugs). Unlike surgery and radiotherapy, chemotherapy is not limited by metastasis. However, anticancer drugs are still unable to destroy all cancer cells in the patient's body so it must still be combined with other treatments such as immunotherapy. The requirements for a good anticancer drug are still difficult to determine because the difference between cancer cells and normal cells is quite small. Treatment with chemotherapy is not selective, so it can affect normal cells, and cause damage.

Cancer treatment with methods such as chemotherapy, immunotherapy, radiotherapy and surgery have side effects that are harmful to the body, and cannot cure cancer completely. Therefore, there is a need for cancer treatment with other methods that are safer, do not cause excessive side effects and are more potent, namely PDT. PDT has been proven to be safe because it is selective, which only kills cancer cells without affecting the surrounding normal cells.

PDT is a treatment that uses special drugs, called photosensitizing agents, which together with light can kill cancer cells. The drugs only work once they are activated by specific light. Photodynamic therapy is a treatment that uses photosensitizer compounds, which selectively accumulate in hyperproliferative target cells followed by local irradiation with visible light. So that the tissue undergoes apoptosis. The mechanism of action of this treatment is described from light absorption to tissue damage.

5. Conlusion

- 1. Cancer or malignant tumors can occur due to the growth of abnormally proliferating cells of body tissues.
- 2. Cancer prevention can be done with healthy living habits and avoiding risk factors that can cause cancer.
- 3. Cancer treatment can be done in 4 ways, namely by surgery, radiotherapy, immunotherapy and chemotherapy.
- 4. Cancer screening can be done with mammography, ultrasonography (USG), and Magnetic Resonance Imaging (MRI).
- 5. Natural ingredients that have effects as cancer prevention and help cancer treatment include Soursop leaves (Annona muricata), Celery leaves (Apium graveolans linn), Red Atai Paku leaves (Angiopteris ferox copel), Benalu Kepel (Dendrophthoe pentandra (L.) Miq.), and Tapak Dara leaves (Catharanthus roseus).

REFERENCES

Ariani, S. 2015, Stop! Kanker. Istana Media, Yogyakarta, Indonesia.

- Andreea, et al. 2011, The Role of Imaging Techniques In Diagnosis Of BreastCancer, J Curr Health Sci, 8: 37-241.
- American Cancer Society. *Mammogram and the other breast imaging tests*[Internet]. 2016 April 25 [cited 2016 July 15].
- Burhan, A., Aisyah, A. N., Awaluddin, A., Zulham, Z., Taebe, B., & Gafur, A. 2019, Uji Aktivitas Antioksidan Dan Antikanker Ekstrak Batang Murbei (Morus Alba L.) Terhadap Sel Kanker Widr Secara in Vitro, *Jurnal Ilmiah Farmasi*, 7(1): 17.
- Brem, et al. 2015, Screening Breast Ultrasound: Past, Present, And Future, AJR Am J Roentgenol, 204(2): 40-234.
- Brown, 2004. Nursing Outcomes Classification, Elsevier, USA.
- Devi, P.U. 2005, *Basics of Carcinogenesis, Health Administrator*, 16 (1): 16-24. Elsyana, Vida et al. 2016, Cytotoxicity and Antiproliferative Activity Assay of
- Clove Mistletoe (Dendrophthoe pentandra (L.) Miq.) Leaves Extracts, Advances In Pharmacological Sciencis, 1(1): 1-6.
- Ezirim AU, Okochi VI, James AB, Adebeshi OA, Ogunnowo S, Odeghe OB. 2013, Induction of Apoptosis In Myelogenous Leukemic K562 Cells by Ethanolic Leaf Extract of Annona Muricata L. Glob J Res Med Plants Indig Med. 2(3):1195–206.
- Fathonah, Rosyidatun. 2018, Identifikasi Efek Samping Kemoterapi Pada PenderitaKanker Di Yayasan Kanker Sindonesia Mulyorejo. *Undergraduate thesis*, Universitas Muhammadiyah Surabaya.
- Foye, 1996. Cancer Chemoterapeutic Agents, American Chemical Society, Washington DC, USA.
- Indah, Y. 2010, Stop Kanker, Agromedia Pustaka, Jakarta, Indonesia.
- Indriyati, 2017. Cegah dan Deteksi Dini Penyakit Kanker, Rumah Sakit Indriyati, Sukoharjo,

Indonesia.

Kowalak. 2011, Buku Ajar Patofisiologi, EGC, Jakarta, Indonesia.

- Lee, *et al.* 2010, Recommendations from The Society Of Breast Imaging And TheACR On The Use Of Mammography, Breast MRI, Breast Ultrasound, And Other Technologies For The Detection Of Clinically Occult Breast Cancer, *JAm Coll Radiol*, 7: 18-27.
- Lodish, Berk, Matsudaira, Keiser, Kreiger, Scott, Zipursky, & Darnell. 2004, *Molecular Cell Biology*, W. H. Freeman and Company , United States of America.
- Lubis, H. 2009, *Dokumentasi Sosial pada Pasien Kanker Perlukah?*, USU Press, Medan, Indonesia.
- Meiyanto, E., Susidarti, R. A., & Handayani, S. 2008, Ekstrak Etanolik Biji Buah Pinang (Areca catechu L.) mampu menghambat proliferasi dan memacu apoptosis sel MCF-7 Ethanolic extract of Arecacatechu seeds inhibit prolifera, Majalah Farmasi Indonesia.
- Raju, J., Patlolla, J. M. R., Swamy, M. V., & Rao, C. V. (2004). Diosgenin, a steroidsaponin of Trigonella foenum graecum (Fenugreek), inhibits azoxymethane-induced aberrant crypt foci formation in F344 rats and induces apoptosis in HT-29 human colon cancer cells. *Cancer Epidemiology Biomarkers and Prevention*.
- Salem, *et al.* 2013, Breast Imaging In The Young: The Role Of Magnetic ResonanceImaging In Breast Cancer Screening, Diagnosis And Follow-Up, *J Thorac Dis*, 5(1): 9-18.
- Sandeep K, Singh BB, Balwinder K, Kuldeep S, Dinesh N. 2013, Research HerbalPlants as Potential anticancer agents: A review, *Journal of Pharmaceutical, Biological and Chemical Sciences*, 4(3): 233-251.
- Sarkar, W., Garrick, H., Kimberly, M., Anuja, O., Shannon, B., Shannon, K., danMcKenna, L., 2013, Cancer Development, Progression, and Therapy: AnEpigenetic Overview, International Journal of Molecular Sciences, 14: 21087-21113.
- Sharma, R., 2012, *Cancer Chemoprevention: Prevention is Better than Cure, Cancer Science Therapy*, S3: e001
- Shukla, A. K., Shasany, A. K., A. Gupta, M. M., & Khanuja, S. 201, Transcriptomeanalysis in Catharanthus roseus Leaves and Roots for Comparative Terpenoid Indole Alkaloid profiles, *Journal of Experimental Botany*, 57 (14): 3921- 3932.
- Suddarth. 2016, Keperawatan Medikal Bedah. Edisi 8. Jakarta: EGC.
- Tong X, Peliing J. 2013, Targeting the PI3K/Akt/mTOR axis by apigenin for cancerprevention, *Anticancer Agents Med Chem*, 13(7): 971–978.
- Verrills, N.M., Walsh, B. J., Cobon, G. S., Hains, P. G., & Kavallaris, M. 2012, Proteome Analysis of Vinca Alkaloid Response and Resistance in Acute Lymphoblastic Leukemia Reveals Novel Cytoskeletal Alterations. *The Journal Of Biological Chemistry*, 278: 45082–45093.
- Van der Heijden, R., Jacobs, D. I., Snoeijer, W., Hallard, D., & Verpoorte, R. 2009, The Catharantine Alkaloids: Pharmacognosy and Biotechnology, *Current Medicinal Chemistry*, 11(5): 607-628.
- Vaughan CL. New developments in medical imaging to detect breast cancer. Breastcancer is still one of the most common cancers in women [Internet]. 2012.
- Wiart C. 2007, Goniothalamus species: A source of drugs for the treatment of cancers and bacterial infection, *Evidence-based Complement Altern Med*, 4(3):299–311.
- Zhou, et al. 2013, Ultrasound Diagnosis Of Breast Cancer, J Med Imaging Health Inform, 3(2):

70-157.