

carcinogenesis.pdf Feb 3, 2022 6291 words / 35914 characters

carcinogenesis.pdf

Sources Overview

7%

OVERALL SIMILARITY

	OVERALL SIMILARITY	
1	Higher Education Commission Pakistan on 2021-07-29 SUBMITTED WORKS	2%
2	Timothy Omara, Ambrose K. Kiprop, Rose C. Ramkat, Jackson Cherutoi et al. "Medicinal Plants Used in Traditional Management of Ca CROSSREF	<1%
3	ERLEND NYBAKK. "LEARNING ORIENTATION, INNOVATIVENESS AND FINANCIAL PERFORMANCE IN TRADITIONAL MANUFACTURIN CROSSREF	<1%
4	Giuseppe Cicero, Tommaso D'angelo, Sergio Racchiusa, Ignazio Salamone et al. "Cross-sectional Imaging of Parotid Gland Nodules: A CROSSREF	<1%
5	De La Salle University on 2022-01-31 SUBMITTED WORKS	<1%
6	Martin Fitzgerald, Michael Heinrich, Anthony Booker. "Medicinal Plant Analysis: A Historical and Regional Discussion of Emergent Co CROSSREF	<1%
7	"Edible Plants in Health and Diseases", Springer Science and Business Media LLC, 2022 CROSSREF	<1%
8	De La Salle University on 2022-01-19 SUBMITTED WORKS	<1%
9	"Plant-derived Bioactives", Springer Science and Business Media LLC, 2020 CROSSREF	<1%
10	Central University of Technology on 2021-11-17 SUBMITTED WORKS	<1%
11	Graceland University on 2019-11-25 SUBMITTED WORKS	<1%
12	Ivy Tech Community College Central Office on 2020-12-02 SUBMITTED WORKS	<1%
13	Manoj Kumar Gupta, Vadde Ramakrishna. "Identification of targeted molecules in cervical cancer by computational approaches", Else	<1%
14	"Catharanthus roseus", Springer Science and Business Media LLC, 2017 CROSSREF	<1%
15	Jhih-Ying Chen, Chia-Min Chen, Pei-Chun Chang, Jeffrey J. P. Tsai. "The Potential Dual-Target Inhibitors for HER2/HSP90 Proteins fro CROSSREF	<1%
16	Kriti Shrinet, Ritika K. Singh, Avinash K. Chaurasia, Alok Tripathi, Arvind Kumar. "Bioactive compounds and their future therapeutic appl CROSSREF	<1%



Universitas Sam Ratulangi on 2021-05-28
SUBMITTED WORKS

<1%

Al-Otibi Fatimah, Raedah Ibrahim Alharbi, Gadah Albasher, Rafa Almeer, Nura Sulaiman Alsaggabi. "Antifungal Potential of Aqueous Ex... <1%

Excluded search repositories:

Internet

Publications

Excluded from document:

Bibliography

Quotes

Citations

Excluded sources:

None

<1%

carcinogenesis.pdf 2/3/22, 9:38 AM

Original Article



Website: www.carcinogenesis.com

10.4103/jcar.jcar_09_21

Medicinal plant in cancer pharmaceutical industry in Indonesia: a systematic review on applications and future perspectives

Jamilah Nasution¹, Eva Sartika Dasopang², Anita Restu Puji Raharjeng³, Kasta Gurning⁴, Gabena Indrayani Dalimunthe⁵, Ikbar Pratama⁶

Abstract:

PURPOSE: This paper aims to write a systematic review paper on the uses, sources, and importance of Medicinal Plants in Cancer Treatments and their role in the Indonesian Pharmaceutical Industry.

METHODOLOGY: This paper is based on Qualitative Research Analysis. Furthermore, it reviews 70 papers based on the conceptual background of Medicinal Plants.

FINDINGS: Medicinal plants have long been used to treat a range of maladies, and they are one of the most important sources of novel pharmacologically active chemicals identified and exploited in the development of new pharmaceuticals by the pharmaceutical industry. Compounds isolated from the Medicinal Plant have been proven to have anti-cancer properties, such as inhibiting cancer cell proliferation and triggering apoptotic cell death.

ORIGINALITY/VALUE: This paper provides knowledge about Medicinal Plants and allows the pharmaceutical industry to practically use the Medicinal Plants to extract the drugs used to cure cancer.

Keywords:

Medicinal Plant, Cancer, Indonesia, Pharmaceutical Industries, Invasion Characteristics, Medical Services.

¹Fakultas Sains dan Teknologi, Universitas Medan Area, Medan, Sumatera Utara, Indonesia ²Fakultas Farmasi, Uni-Indonesia ³Fakultas Saintek, UIN Sekolah Tinggi Ilmu Kesehatan Senior Medan, Indonesia Utara, Indonesia gmail.com; ikbar.p@gmail.

Accepted: 28-Jun-2021

Introduction

The medicinal plant in the cancer versitas Tjut Nyak Dhien, which is still in its infancy, can grow into a big market.[1] This paper systematically Raden Fatah Palembang, reviewed the applications of medicinal Indonesia plants in cancer pharmaceuticals and ⁴Departemen Farmasi, future perspectives that the government is considering. This paper aimed to Indonesia systematically review the applications of ⁵Faculty of Pharmacy, medicinal plants in cancer pharmaceuticals Universitas Muslim and future perspectives considered by the Nusantara AL Washliyah, Indonesian government. The inclusion ^oFakultas Ekonomi dan criteria were based on scientific evidence Bisnis, Universitas Medan or reports published in scientific journals. Area, Medan, Sumatera [2] The exclusion criteria are applied when

Corresponding author: jamilah.nasution83@ This is an open access journal, and articles are distributed inder the terms of the Creative Commons Attribution-Submitted: 21-Mar-2021
Revised: 13-Jun-2021
Reverted: 20 in 2021

Published: 12-Oct-2021 For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

there is no scientific evidence for the use of plant extract in cancer treatment. In addition, they are either not used medicinally or contain any relevant phytochemicals for anti-cancer purposes.

Cancer is one of the deadly diseases and it is causing second highest deadliest mortality rate after cardio diseases. Efforts in drug discovery and development are still struggling to provide effective treatments for patients with cancer. Medicinal plants have used as a natural source of drugs against cancer and other diseases. Botanical products derived from plants have vast anti-cancer activities, some of which are investigated due to limited investigation options by biomedical researchers.[3] However, recent advances in genomic

How to cite this article: Nasution J, Dasopang E S, Raharjeng A R P, Gurning K, Dalimunthe G I, Pratama I. Medicinal plant in cancer pharmaceutical industry in Indonesia: a systematic review on applications and future perspectives. J Carcinog 2021;20:21.

© 2021 Journal of Carcinogenesis | Published for Carcinogenesis Press by Wolters Kluwer - Medknow

Nasution, 2 al.: Medicinal plant in cancer pharmaceutica industry in Indonesia

techniques allow the identification of molecular targets involved in the modulation and control of plant gene expression to identify new medicinal properties from plants, which would be of great importance for pharmaceutical industries. [4] Cancer is one of the major problems in all countries including developing and developed countries both. There are many efforts to develop new cancer treatments in the pharmaceutical industry, including medicinal plants. [5]

The use of Medicinal Plants (MP) in the pharmaceutical industry has proposed as a low-cost alternative to synthetic drugs and other more expensive treatments. [6] Every year around 1.8 percent people out of 100,00 persons are suffering from cancer worldwide and almost 100 people die by cancer every day. According to the report of world health care organization, every year there are more than fourteen million people suffer from cancer and out of them eight million people die by cancer all over the world. Indonesia has a high cancer rate as indicated by the R/D ratio (1.3/1.000)people). From 2013 to 2014, there were 82,500 ew cases of cancer in Indonesia and 3.2 million deaths from the disease. The main etiologies are tobacco use, alcohol use and radioactive fallout from nuclear tests conducted by the U.S. in the 1950s. [7] It also involves the use of pesticides and industrial pollution, which was considered as one of the major causes for cancer. These factors ultimately led to an increase in cancer cases in Indonesia. Cancer is the second leading cause of death in Indonesia, after stroke. Cigarette smoking and alcohol consumption are the major risk factors. In Indonesia, cancer incidence has increased by 4.5% per year in men and 1.9% per year in women since 1980 (1). The major risks for tobacco use are lung cancer and bronchc-oesophageal cancers (5/100,000), breast cancer (3/100,000) and liver cancer (3/100,000). hepatoblastoma and melanoma are responsible for 2/100,000 people per year. There is a wide range of human health damages to the environment caused by industrial pollutants. The main pollutants are: air pollutants, household and food chemicals and radioactive fallout from nuclear tests performed by the U.S. in the 1950s. [8] Air pollution occurs due to two major factors: overall emissions due to consumption of fuels; vehicle emissions include exhaust-gas emission, hydrocarbon-emission and nitrogen oxide pollutant; household air pollution includes indoor exposure to chemical substances (including pesticides and pesticides with high indoor concentrations). Amongst these chemicals, DDT (dichlorodiphenyltrichloroethane) presents multiple risks for health effects, including carcinogenicity.[9]

Plants are producing a complete and different range of chemical compound that doesn't have any direct role in the growth of plants. When these chemicals are extracted from plants for medicinal purposes, they are known as phytochemicals or medicines of plant origin. The secondary metabolites are the plants' genetic potential products to produce many chemical compounds that were not necessarily needed to survive and reproduce. The idea that phytochemicals can used to treat humans is not new.[9] They have been used for thousands of years as medicines, food preservatives, dyes, perfumes and insecticides. The growth of research into phytochemicals and their use in medicine has been driven by various factors, including chemists' discovery of various complex structures for these substances and research into traditional medicines using modern scientific methods. This is also known as ethnomedical research. Examples include studies conducted by the World Health Organization and the advances in medical technology through which phytochemicals can be harvested without harming animals.[10] The high proportion of secondary metabolites in plants has led to ethno medicine's decreased scope within modern medicine since medicinal plants containing valuable substances have been replaced with synthetic drugs. However, there is evidence that ethno medicine is undergoing a revival due to new technologies for harvesting chemicals from plants and growing awareness of their importance in modern pharmacology.[11] Indonesia has a long history of using native plants to treat disease, and it is estimated that only 5% of the country's medicinal plants have been researched. According to a study conducted in Indonesia by Biswas and McDermott, the benefits of using native medicinal plants over those synthetic medications may be attributed to their efficacy as treatments and their low cost, as well as the plant's traditional reputation for being both safe and effective.[12]

Studies conducted on overseas tropical forests have shown that most medicines of plant origin are used for traditional purposes such as treatment for illness or for curing physical or mental problems.[13] The development of new drugs is a lengthy process that starts with an idea for a potential drug and eventually progresses through testing on animals before it is tested on people. Still, this new study suggests that some time should be spent on medical research into the health benefits of plants before animal testing. This review paper will cover current applications in cancer pharmaceutical industry in Indonesia focusing mainly on anti-cancer activity, chemo preventive activity, immunomodulatory activity, antimicrobial activity and wound healing properties.[14] The positive impact of plants in cancer treatment have been completely d it has shown positive results. There studies a are many nedicinal plants used in the treatment of cancer, including traditional folk medicine to modern medicines. This study analyzed the utilization and future perspectives for medicinal plants in the

Nasution, et al.: Medicinal plant in cancer pharmaceutica dustry in Indonesia

pharmaceutical industry in Indonesia. Controlling the disease, improving health, and being an integral part of Indonesian culture, eventually involves cancer treatment. Medicinal plants in cancer treatment have been reported in many countries, including Asia. Growth in medicinal plant use for cancer treatment has occurred from ancient times to the present day. [6] This is mainly due to their traditional and modern applications. Their effect in different aspects such as their pharmacological values, biochemistry properties, and efficacy for treatment are well known and investigated. Also, they can be used as adjuvant or presented as future drugs.

Literature Review

Cancer ascribes a collection of diseases triggered by the uncontrolled proliferation of malignant cells. Cancer ascribes a collection of diseases triggered by the uncontrolled proliferation of malignant cells in Indonesia.[9] This study is focused on the medicinal plant in the cancer pharmaceutical industry, which is used in Indonesia. There are many options to choose from, but this review will only focus on this plant's applications and future perspectives. The information about current knowledge about the medicinal plant and its potential for use as medicine comes from published articles that can be found online, such as journals and books. Recently, there has been research on many medicinal plants that might help with cancer treatment. [15] This article reviews some of them with their uses and future perspectives in our country. Unfortunately, these areas are often neglected or overlooked because they are outside conventional scientific research due to their economic value or lack of funding. Currently, the Government of Indonesia is trying to control medicinal plants in cancer chemotherapy.[16] This will allow for more research on their therapeutic applications, mainly since so many plants have been used in cancer treatment throughout time. This study explains how medicinal plants in cancer pharmaceutical industry are used and researched as medicine. It is also discussed on how they are being promoted as medicines that can lead to more research and development. It also shows how they could be effectively worked into pharmaceutical companies' research process if accepted by society and endorsed by the government. Several studies have been carried out to evaluate which type of nutraceutical or phytomedicines shows potential for application in cancer therapy.[2] is a global health burden that has left an intolerable death toll worldwide. Conservative estimates indicate that cancer (of the liver, breasts, lungs, cervix uteri, stomach, and colorectal) causes about 13% of annual deaths in Indonesia. Indonesia is a country with a large and diverse ethnical and linguistic population; it has been estimated that as many as 300 ethnic groups live there. Some of these ethnic groups

have their own traditional medicine systems, including the Javanese who have developed a unique and complex medical system based on herbs and natural products.^[9]

Traditional medicinal plants are still actively used in most Indonesian regions (e.g., Sumatra, Kalimantan, Sulawesi, Java), with reported total usage rate of about 80%. The total number of plant species used for medicinal purposes in Indonesia (including medicinal parts of plants) has been estimated at about 65 00-70 000 species. [17] In addition to traditional medicines, modern pharmaceutical drugs are also quite common.

In Indonesia, the total cancer pattern is still dominated by lung cancer (31.2%), followed by breast cancer (22.0%) and stomach cancer (12.7%). Lung cancer is still the major cause of death due to cancer in every year, followed by breast and stomach cancers. The death rates related to cancer are decreasing more rapidly now, so the burden of various cancers is probably more severe than before. Nowadays, Indonesia has an estimated population of 260 million people that include 22% females and 78% males (for reference). Approximately 29% of them live in urban districts and 71% live in rural districts. In Indonesia, the majority of cancer cases are suffering from tobacco-related cancers (60%).[18] In Indonesia, around 86% people develop cancer through tobacco use over an average period of nearly 11 years. While the highest cancer incidence rates in 2016 were in the 27-44 age group, accounting for 8.3% of all cases and 12.6% of total deaths.^[19] The mortality rate of cancer patients (15.6 per 100,000 people) has been increasing significantly since 2011, with the highest mortality rate in males (21.1 per 100,000 people). The median age at death is 62 years for men and 67 for women. Malignant tumors and hematologic cancers are the most common causes of death among people aged between 55-69 years (male) and 70-84 years (female).[15]

Cancer is not solely a disease of developed country but also a problem for developing countries. Cancer shows the same threat and risk in all countries, but cancer occurrence is not equal due to the different living habits and nutrition in different regions. For instance, breast cancer is more common in Indonesia among women (22.0%), especially those residing in Java Island. On the other hand, like most Asian countries lung cancer is more prevalent among men (31.2%).[8] The most common cancer in Indonesia is lung cancer with 76,717 new cases each year followed by stomach cancer which accounts for 20% of new cases per year reported according to The Ministry of Health in 2013. In Indonesia, cancer is still a significant illness that causes health problems among the public. The most common cancers in Indonesia ranked lung cancer (46.8%), breast cancer (22.0%), and stomach cancer (12.7%). Besides this, other diseases are among the top ten causes of

Nasution, et al.: Medicinal plant in cancer pharmaceutica dustry in Indonesia

death in Indonesia, namely: cardiovascular disease, HIV/AIDS-related malignancies, and diabetes mellitus. [16] In 2013 alone, more than 60,000 people died because of malignant neoplasms or tumors. Furthermore, it is estimated that there were 191 new lung cancer cases per 100,000 individuals in 2013. In addition, estimations of 2010 showed that lung carcinoma has the highest mortality rate with 42.54% of deaths were due to the disease in 2007.[14] In Indonesia, the cancer burden is not equal. The most prevalent cancers are lung cancer and stomach cancer, which are more common among men and women. In addition, these two cancers are also the primary causes of death. Overall, the percent mortality from all types of cancers was 1.132 per 100,000 between 2008 to 2010. Therefore, there is a huge need for effective preventive measures for various types of cancers in Indonesia to reduce mortality rates of cancer patients as well as to improve quality of life for people who have developed some forms of cancer. For example, in 2013, the number of new cancer cases reported was 191 per 100,000 people aged 0 to 79 years. [13] The data shows that lung (92.1%) and breast (14.6%) cancer are the country's most common forms of cancer. On average, about 13 million inhabitants in Indonesia during 2010.[19] Many studies have been conducted for breast tumor patients because breast cancer is complicated.

In addition, studies have shown many cases with another form of cancer, such as brain tumors and leukemia, among women diagnosed with breast tumors. [14] There is a huge need for effective preventive measures for various types of cancers in Indonesia to reduce mortality rates of cancer patients and improve quality of life for people who have developed some forms of cancer. [8]

Methodology

This systematic review paper supports the use of Medicinal Plants in treating cancer and other disorders. The keywords used to search relevant research papers were Medicinal Plant, Cancer, Indonesia, Pharmaceutical Industries, Invasion Characteristics, Tumor Cells, and Cancer Treatment.[20] The main goal for choosing this topic is to study the role of Medicinal Plants in Cancer Treatments and how Medicinal Plants can help treat other disorders. The reason for studying the medical and pharmaceutical aspects is that Medicinal Plants are sources of Natural Products. Previous research has revealed that natural sources are one of the primary sources of pharmaceuticals. [2,9] In Pharmaceutical Industry, medicinal plants being the most prominent source of natural products. This systematic review paper will review the use of Medicinal Plants for cancer treatments in Indonesia. This paper will also review the application of Medicinal

Plants and how they can play their role in the future. The primary concern of this paper is reviewing the use and sources of Medicinal plants. Therefore, it was found in previous studies that Medicinal Plants have been used in folk medicine in African and Asian populations for thousands of years, and many of these plants are taken for their health advantages in modern countries as well.[4] According to reports and a news brief from the WHO (World Health Organization), some countries continue to rely on plant-based treatment as their primary source of medication, whilst developing countries are increasingly realizing the medicinal potential of organically produced compounds. However, Brassinosteroids, Taxol and Polyphenols are some of the anticancer compounds found in Medicinal Plants. The goal of this systematic review paper was to find out how important medicinal plants are in the pharmaceutical industry and how they are used and where they come from. The criteria of research were based on the selected keywords. The research technique used for this systematic review work on Medicinal Plants. This paper is based on research papers from 8 impact factor journals, as depicted in Figure 1.[10]

Table 1: Impact Factor Journals

Sr. No	Impact Factor Journals	H. Index	No. of Selected Articles
1	The American Journal of Medicine	229	10
2	Nature Reviews Immunology	390	13
3	New England Journal of Medicine	1030	8
4	MMWR Recommendations and Reports	143	12
5	Journal of Clinical Oncology	548	11
6	Annual Review of Pathology: Mechanisms of Disease	122	6
7	Annual Review of Clinical Psychology	117	5
8	Journal of Experimental Medicine	448	5
Total			70

After conducting a comprehensive study of the literature on the relationship between medicinal plants' use, source, and relevance in the Indonesian Pharmaceutical Industry, the review paper was written. Furthermore, the paper has selected a limited number of papers, as shown in table 2 and figure 2. The impact factor journals with a higher medical publications index were used to screen out quality papers. These journals were the American Journal of Medicine, New Reviews Immunology, New England Journal of Medicine, MMWR Recommendations and Reports, Journal of Clinical Oncology, Annual Review of Pathology, Annual Review of Clinical Psychology,

Nasution, et al.: Medicinal plant in cancer pharmaceutica dustry in Indonesia

and Journal of Experimental Medicine. The H Index of the selected journals is mentioned in Table 1. The research summary for this study is shown in Table 2;

after selecting high-impact factor journals, efficient keyword selection was performed to obtain targeted results.

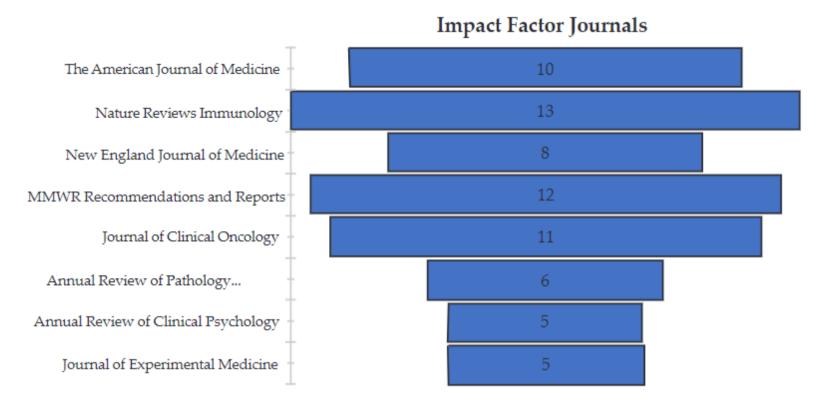


Figure 1: Impact Factor Journals

By using these search filters, I have scanned the summary of this research. Filters were used to ensure that the results were correct. Only qualitative research was chosen because systematic qualitative review keeps the aim on topic, and systematic argument over the necessity to be exhaustive brings the goal on topic. I studied and examined the complete text of the selected papers and resources and then extracted

the essential information pertinent to my review paper on Medicinal Plants and their uses, source and importance in Pharmaceutical Industry. This study's inclusion/exclusion criteria were based upon Figure 2, which demonstrates that publications were searched according to specified keywords to produce appropriate results. The time was filtered between 2017-2021.^[5]

Table 2: Research Summary of Paper

Journals Searched	Searched Keywords	Limits	initial Results	End Results	Selected Papers
The American Journal of Medicine	Medicinal Plant, Cancer.	Publication Date: 2017 to 2021	321	14	10
Nature Reviews Immunology	Medicinal Plant, Indonesia, Pharmaceutical Industries, Cancer	Content-Type: Articles Publication Date: 2017 to 2021	94	40	13
New England Journal of Medicine	Medicinal Plant, Cancer, Indonesia, Pharmaceutical Industries.	Publication Date: 2017 to 2021	50	19	8
MMWR Recommendations and Reports	Medicinal Plant, Cancer, Indonesia, Pharmaceutical Industries, Medical Services.	Publication Date: 2017 to 2021	23	15	12
Journal of Clinical Oncology Annual Review of	Medicinal Plant, Cancer, Indonesia, Pharmaceutical Industries, Invasion Characteristics, Medical Services.	Publication Date: 2017 to 2021	30	20	11
Pathology: Mechanisms	Medicinal Plant, Cancer, Indonesia.	Publication Date: 2017 to 2021	94	18	6
of Disease Annual Review of	Medicinal Plant, Cancer, Indonesia, Medical Services.	Publication Date: 2017 to 2021	213	12	5
Clinical Psychology Journal of Experimental	Medicinal Plant, Cancer, Indonesia, Pharmaceutical	Publication Date: 2017 to 2021	86	10	5
Medicine Journal of Experimental Medicine	Industries, Medical Services. Medicinal Plant, Cancer, Indonesia, Pharmaceutical Industries, Medical Services.	Publication Date: 2017 to 2021	86	10	5

After selecting the impact factor journals, the database was searched with keywords (as mentioned in Table 2). The searched keywords were applied filter. For example, on the website of The American Journal of Medicine, after writing the keywords (Medicinal

Plants, Cancer), where 321 results were found. After that, research filters were applied as Publication Data: 2017 to 2021. The results were 14. However, only ten papers were selected for further research purposes after screening articles. Research Filters were applied

Nasution, et al.: Medicinal plant in cancer pharmaceutica dustry in Indonesia

to the keywords. Only a few publications were selected from the 20th century, just for the in-depth analysis of the theory progression and startup. Figure 2 illustrates that only 70 articles and resources were picked in the qualitative research synthesis. Furthermore, on the Journal of Clinical Oncology website, after writing the keywords (Medicinal Plant, Cancer, Indonesia, Pharmaceutical Industries, Invasion Characteristics, Medical Services), 30 results were found. After that, research filters were applied as Publication Data: 2017 to 2021. The results were 20. However, only 11 papers were selected for further research purposes after screening articles. 8 Journals were selected, and a total of 70 papers were selected.

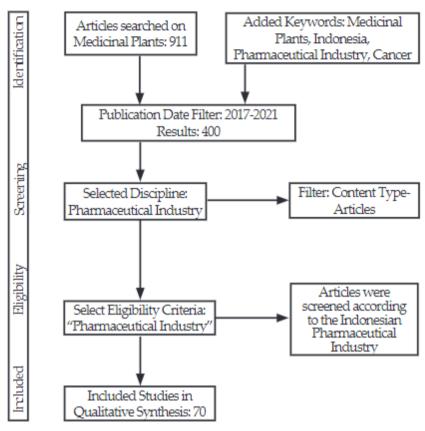


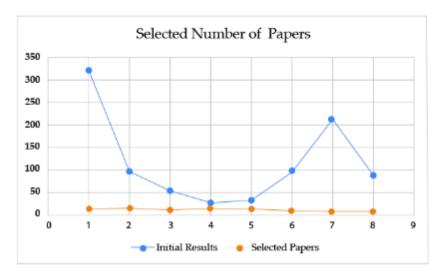
Figure 2: Article Inclusion Criteria

I have chosen the period 2017-2021 to investigate the role of Medicinal Plants in developing the Pharmaceutical Industry in the twenty-first century. After applying all of the filters, only those articles with the needed keywords were picked. Only 70 articles and research papers were selected for the qualitative synthesis phase.

Table 3: Selected Number of Paper

Impact Factor Journals	Initial Results	Selected Papers
The American Journal of Medicine	321	10
Nature Reviews Immunology	94	13
New England Journal of Medicine	50	8
MMWR Recommendations and Reports	23	12
Journal of Clinical Oncology	30	11
Annual Review of Pathology	94	6
Annual Review of Clinical Psychology	213	5
Journal of Experimental Medicine	86	5
Total Selected Papers	911	70

The data collection period was set between 2010 and 2021, although just a few papers from the twentieth century were used to examine the evolution and history of theory. Figure 3 depicts the number of publications published between 1975 and 2021.



The problem stated in the study is that there are many different types of cancer in the human population. [21] This is the study's solution statement. In spite of this, they all have certain characteristics or genotypes in common, such as an increased sensitivity to signals that interfere with cell growth, which permits them to replicate. In addition, angiogenesis is maintained within the tumor tissue, which allows for the survival of cancer cells by evading and never inducing apoptosis in them. Plant-derived chemicals have been shown to exhibit qualities that limit cancer cell activity, such as suppressing cancer cell proliferation and inducing apoptotic cell death.

Historical Background

From documented history, we have learned about ancient medical expertise. Since then, it has been treasured and disseminated in every corner of this civilized world. The herbal and natural sciences were responsible for nearly every ancient drug discovery.[1] Natural chemicals are used to make or extract the bulk of significant medicines. Natural goods or derivatives of natural products account for more than one-third (39.1%) of all FDA-approved medications. In comparison, natural goods or derivatives account for 48.6% of all cancer drugs registered from the 1940s to the present.[22] In the drug discovery process, naturopathic goods are a great source of knowledge. Even though there are more than 200,000 different naturally occurring metabolites with different bioactive properties, natural products' relevance in identifying novel medications cannot be overstated.[23] Medicinal lants are an excellent source of natural products, and they are one of the most often used. Medicinal plants have been utilized for therapy in almost every country from ancient times and continue to be used now. Plantbased traditional medicinal methods and a century of beliefs and observations have influenced modern

Nasution, et al.: Medicinal plant in cancer pharmaceutica addustry in Indonesia

medicine. In order to defend themselves, plants have created a sophisticated defensive mechanism that includes a diverse array of compounds. [3] Long ago, it was recognized that antimicrobial compounds in plant tissues were significant in producing natural products. These compounds could also be utilized to fight infections that cause human disease as botanical pesticides or as bactericidal and fungicidal agents. [7]

Indonesian Pharmacist states that Medicinal Plants have long been used to treat a range of diseases, and they are one of the most important sources of novel pharmacologically active chemicals identified and exploited in the development of new pharmaceuticals by the pharmaceutical industry.[24] Between 35,000 and 70,000 plant species have been researched for their possible therapeutic value in the modern day. Plants with ethnopharmacological uses served as key sources of medicine for generating medications related to those ethnopharmacological uses in the early stages of drug development.[11] The search for medications derived from plants today is based on the bioactivity of the plants, which has resulted in the discovery of significant anticancer treatments such as paclitaxel and camptothecin.

Sources of Anti-Cancer Drug

Because they are natural and widely available, plant-derived medications are highly sought after for cancer treatment. They are practical since they can be administered orally as part of a patient's daily regimen.

[25] Furthermore, they are usually more tolerant and non-toxic to normal human cells than synthetic drugs because they are made naturally from plants. Exceptions, such as saponins, lignans, lectins, taxanes, cyanogenetic glycosides, and lectins.
[26] Assume that in research, plant-derived drugs are demonstrated to be selective, non-toxic to normal cell lines, and cytotoxic to cancer cell lines. These medications can then be examined in clinical trials to aid in identifying new cancer treatment agents.
[25] The most frequent category of plant-derived medicine is methyltransferase inhibitors.

HDAC inhibitors include compounds such as sulforaphane, isothiocyanates, isoflavones, and pomiferin, among others, that inhibit the enzyme HDAC.^[24] They work by preventing carcinogenic proteins from functioning. For example, sulforaphane has been demonstrated to suppress the activity of critical targets in the growth of breast cancer. In breast cancer cell lines, sulforaphane reduced estrogen receptor ^[3], epidermal growth factor receptor, and human epidermal growth factor receptor-2. HDAC inhibitors allow cancer cells to reach a state known as programmed cell death (PCD) by reactivating epigenetically repressed genes involved in chromatin acetylation (apoptosis). The use of plant-derived

chemicals that inhibit the HDAC enzyme in cancer cells can improve the sensitivity of cancer cells to chemotherapy treatments.^[6]

Demand of Medicinal Plants in the Indonesian Pharmaceutical Industry

Plant-based medications are becoming more appealing for clinical development due to successful clinical trials. Because of their non-toxic effects on healthy cells and cytotoxic effects on cancer cells are popular among scientists.[8] Many of the species researched come from underdeveloped African and Asian countries where herbal therapy is practiced and medicinal plants are employed as primary therapies.[27] The World Health Organization estimated the value of the plant-derived pharmaceutical trade to be at US\$100 billion in 2007. It is estimated that global trade would exceed \$5 trillion by 2050.[28] There is a high demand for medicinal plants in emerging countries, putting a strain on plant populations' resources. Many therapeutic plants are produced from wild populations for the illegal market, but no official agency controls the process. With population growth, deforestation, and urbanization on the rise, medicinal plant protection is becoming a critical issue that needs to be handled right away. If overexploitation continues as a result of rising demand, high-value medicinal plants may become extinct. These plants need to be saved.

Criticism

Supercritical Fluid Chromatography (SFC) is a technique for separating supercritical fluids from ordinary water. SFC is a liquid-based chromatographic technique that utilizes a stationary phase of low pressured viscosity (supercritical) fluids, most often carbon dioxide (SFC). It has progressed significantly since its debut by Klesper in 1962, owing primarily to advances in instrumentation, which was initially troublesome. It has the specific advantage of being particularly useful for separating intricate components characteristic of natural molecules when compared to other techniques. A variety of polarities, ranging from non-polar to polar, can be used to fine-tune the selection of the optimal circumstances for SFC mobile phases and modifiers, allowing for a wide range of separations. Polarities can be used to finetune the selection of the ideal circumstances for SFC mobile phases and modifiers. Only a few years after SFC was first hyphenated with gas chromatography, it was used to analyses natural compounds for the first time. Several natural compounds found in herbal medicines have recently been added to the list, with a particular emphasis on terpenes, polyphenolics, flavonoids (including flavonols), alkaloids (including alkaloids), and saponins (among other things). It has been used to aid in developing MS systems, liode array detectors,

Nasution, et al.: Medicinal plant in cancer pharmaceutical industry in Indonesia

SFC-ELSD systems, and the identification of novel stationary phases such as cyanopropyl, pentafluoro phenyl (PFP), and imidazolyl, to name a few areas of application.

Conclusion

Only certain plant components are frequently employed in therapy when wild medicinal herbs are obtained. Only a little portion of a plant is harvested, causing damage and reducing the plant's ability to survive. A comprehensive treatment approach that includes all plant parts (including the stem, leaf, root, and bark) must be implemented to ensure medicinal plants' long-term viability in poorer nations. Other options for germplasm preservation include storing viable seeds, cryopreservation, maintaining biological material in liquid nitrogen, and tissue culture, in addition to germplasm preservation. Plants may be propagated in sterile circumstances, and tissue culture can be used to make clones of rare species in a relatively short period of time, which is particularly useful for conservation efforts. These preservation processes will also make it possible for industrial applications to be implemented in developed areas. To meet the growing demand for natural alternatives to pharmaceuticals, ome medicinal plants are being grown on a large scale in industrialized countries such as Europe, Indonesia, and China, among other places. Cultivating sustainable species can relieve pressure on other wild species while also aiding in the prevention of plant species extinction. Land that could otherwise be used for other agricultural purposes may become overburdened due to mass farming, though.

Future Recommendations

Phere has been an increase in interest in medicinal plant research and analysis, as seen by the more than threefold increase in the number of recent publications, from 3242 in 2017 to 664 in 2021. Since the included database records began in 1880, output released during the first eight years of this decade alone surpassed all those published before 2001. Over the preceding ten years, the fields of pharmacology and pharmacy have accounted for most articles cited in current databases for medicinal plant analysis reports. Plant sciences, biochemistry, molecular biology, and agriculture research come in second and third, respectively, accounting for nearly 70% of all publications.

References

- Akhtar N, Mirza B. Phytochemical analysis and comprehensive evaluation of antimicrobial and antioxidant properties of 61 medicinal plant species. Arab J Chem 2018; 11:1223-35.
- Al-Tohamy R, Ali SS, Saad-Allah K, Fareed M, Ali A, El-Badry A, El-Zawawy NA, Wu J, Sun J, Mao G-H. Phytochemical analysis and assessment of antioxidant and antimicrobial

- activities of some medicinal plant species from Egyptian flora. J Appl Biomed 2018; 16:289-300.
- Dash SP, Dixit S, Sahoo S. Phytochemical and biochemical characterizations from leaf extracts from Azadirachta Indica: an important medicinal plant. Biochem Anal Biochem 2017; 6:1-4.
- Hassan A, Ullah H. Antibacterial and antifungal activities of the medicinal plant veronica biloba. Journal of Chemistry 2019; 2019:1-7.
- Heinrich M, Anagnostou S. From pharmacognosia to DNAbased medicinal plant authentication-pharmacognosy through the centuries. Planta Med 2017; 83:1110-6.
- Jeelani SM, Rather GA, Sharma A, Lattoo SK. In perspective: Potential medicinal plant resources of Kashmir Himalayas, their domestication and cultivation for commercial exploitation. Journal of applied research on medicinal and aromatic plants 2018; 8:10-25.
- Kayser O. Ethnobotany and medicinal plant biotechnology: from tradition to modern aspects of drug development. Planta Med 2018; 84:834-8.
- Majolo F, Delwing LKdOB, Marmitt DJ, Bustamante-Filho IC, Goettert MI. Medicinal plants and bioactive natural compounds for cancer treatment: Important advances for drug discovery. Phytochemistry Letters 2019; 31:196-207.
- Oyenihi A, Smith C. Are polyphenol antioxidants at the root of medicinal plant anti-cancer success? J Ethnopharmacol 2019; 229:54-72.
- Sawicka B, Skiba D, PszczóA P, Aslan I, Sharifi J, Krochmal-Marczak B. Jerusalem artichoke (Helianthus tuberosus L.) as a medicinal plant and its natural products. Cellular and Molecular Biology 2020; 66:160-77.
- Singh S, Singh DB, Singh S, Shukla R, Ramteke PW, Misra K. Exploring medicinal plant legacy for drug discovery in postgenomic era. Proceedings of the National Academy of Sciences, India Section B: Biological Sciences 2019; 89:1141-51.
- Jamshidi-Kia F, Lorigooini Z, Amini-Khoei H. Medicinal plants: Past history and future perspective. Journal of herbmed pharmacology 2018; 7:1-7.
- Shikov AN, Narkevich IA, Flisyuk EV, Luzhanin VG, Pozharitskaya ON. Medicinal plants from the 14th edition of the Russian Pharmacopoeia, recent updates. J Ethnopharmacol 2021; 268:113685.
- Tungmunnithum D, Thongboonyou A, Pholboon A, Yangsabai A. Flavonoids and other phenolic compounds from medicinal plants for pharmaceutical and medical aspects: An overview. Medicines 2018; 5:1-16.
- Hussein RA, El-Anssary AA. Plants Secondary Metabolites: The Key Drivers of the Pharmacological Actions of Medicinal Plants. In Herbal Medicine, Builders PF (eds.). IntechOpen. 2018, pp. 11-30.
- Shedoeva A, Leavesley D, Upton Z, Fan C. Wound healing and the use of medicinal plants. Evid Based Complement Alternat Med 2019; 2019:1-30.
- Adhikari B, Marasini BP, Rayamajhee B, Bhattarai BR, Lamichhane G, Khadayat K, Adhikari A, Khanal S, Parajuli N. Potential roles of medicinal plants for the treatment of viral diseases focusing on COVID-19: A review. Phytother Res 2021; 35:1298-312.
- DeFilipps RA, Krupnick GA. The medicinal plants of Myanmar. PhytoKeys 2018: 1–341.
- Khan T, Khan MA, Ullah N, Nadhman A. Therapeutic potential of medicinal plants against COVID-19: The role of antiviral medicinal metabolites. Biocatalysis and Agricultural Biotechnology 2021; 31:101890.
- Tambunan USF, Parikesit AA, Nasution MAF, Hapsari A, Kerami D. Exposing the molecular screening method of Indonesian natural products derivate as drug candidates for cervical cancer. Iranian journal of pharmaceutical research: IJPR 2017; 16:1113–27.
- Mohiuddin AK. An AZ Pharmaceutical Industry: Bangladesh Perspective. Asian Journal of Research in Pharmaceutical Science 2019; 9:17-28.

Nasution, et al.: Medicinal plant in cancer pharmaceutical industry in Indonesia

- 22. Li F-S, Weng J-K. Demystifying traditional herbal medicine with modern approach. Nature plants 2017; 3:1-7.
- Jahn L, Schafhauser T, Wibberg D, Rückert C, Winkler A, Kulik A, Weber T, Flor L, van Pée K-H, Kalinowski J. Linking secondary metabolites to biosynthesis genes in the fungal endophyte Cyanodermella asteris: The anti-cancer bisanthraquinone skyrin. J Biotechnol 2017; 257:233-9.
- Ashraf MA. Phytochemicals as potential anticancer drugs: time to ponder nature's bounty. BioMed research international 2020; 2020:1-7.
- 25. Barkat MA, Goyal A, Barkat HA, Salauddin M, Pottoo FH, Anwer
- ET. Herbal Medicine: Clinical Perspective and Regulatory Status. Combinatorial Chemistry & High Throughput Screening 2021; 24:1573-82.
- Kintzios SE, Barberaki MG. Plants that fight cancer. Crc Press. 2019.
- Kuruppu A, Paranagama P, De Silva R. Anticancer potential of natural products: a review focusing on Sri Lankan plants. Frontiers in bioscience (Scholar edition) 2019; 11:161-77.
- Akhtar MS, Swamy MK. Anticancer plants: natural products and biotechnological implements. vol. 2. 1st edn. Springer. 2018.