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The Antiangiogenic Activity of Alokon (*Broussonetia luzonica*) Flower Extract Using Chick Chorioallantoic Membrane (CAM) Assay

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ABSTRACT

Cancer remains a leading cause of mortality worldwide, with existing treatments often being costly and accompanied by adverse effects. This study investigated the antiangiogenic activity of Alokon (Broussonetia luzonica) flower extract as a potential natural alternative for inhibiting blood vessel formation critical to tumor growth. Using the Chick Chorioallantoic Membrane (CAM) assay, the study evaluated blood vessel inhibition across six treatment groups: distilled water (negative control), Quercetin (positive control), and four extract concentrations (25%, 50%, 75%, and 100%). Results demonstrated that Alokon extract exhibited a dose-dependent inhibition of angiogenesis, with the 100% concentration achieving comparable efficacy to Quercetin (27.87% and 29.60% inhibition, respectively). Statistical analyses, including ANOVA and Scheffé test, confirmed significant differences between treatment groups, highlighting the extract's potential as a cost-effective antiangiogenic agent. These findings highlight the value of Alokon flower extract in developing accessible cancer therapies, warranting further exploration into its bioactive compounds and therapeutic applications.

Keywords: *Antiangiogenic Activity, Alokon, Chorioallantoic Membrane, IKOSA*

INTRODUCTION

Cancer is a life-threatening disease and a leading cause of death worldwide, including in the Philippines, where it ranks as the second leading cause of mortality (Lagarde et al., 2019; WHO, 2022). Cancer progression heavily relies on angiogenesis, the formation of new blood vessels that provide tumors with oxygen and nutrients necessary for their growth and metastasis (Jaywant et al., 2011). This process is driven by complex signaling pathways, including the vascular endothelial growth factor (VEGF), which regulates endothelial cell proliferation and capillary network formation (Herrera & Amor, 2011). While chemotherapy and radiotherapy have shown efficacy, their high costs and significant side effects limit their

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accessibility, especially in resource-limited settings like the Philippines (Baclig, 2023). These challenges highlight the urgent need for affordable and effective alternatives.

The use of medicinal plants in traditional medicine provides a valuable foundation for developing new therapies. Many modern drugs have roots in plant-derived compounds, which have been shown to disrupt angiogenesis pathways critical for tumor growth (Egbuna, 2018; Hazafa et al., 2020). In Ilocos Sur, ethnomedicinal and ethnobotanical studies have documented the extensive use of plants for therapeutic purposes. Domingo (2022) explored the diverse ethnomedicinal practices in the region, highlighting the community's reliance on plant-based remedies. Bañez (2022) demonstrated the ethnobotanical value of medicinal plants in managing vector-borne diseases like dengue, while Corpuz (2020) investigated the antifungal properties of mangosteen and pomegranate, showcasing their pharmacological significance. Building on these studies, this research examines Alokon (*Broussonetia luzonica*), a plant with both culinary and traditional medicinal importance, as a potential natural antiangiogenic agent.

Alokon is a medium-sized tree native to the Philippines, known for its edible inflorescences and ecological benefits such as erosion control and reforestation (Philippine Bureau of Plant Industry, 2019). Previous studies on related Broussonetia species have identified a rich phytochemical composition, including flavonoids, alkaloids, and polyphenols, which exhibit antitumor, antioxidant, and anti-inflammatory properties (Chen et al., 2022). Despite the wealth of research on these species, the antiangiogenic activity of Alokon remains largely unexplored, representing a critical gap in the literature. The potential of Alokon as a source of natural bioactive compounds could address the limitations of existing cancer therapies by offering an affordable and accessible alternative.

Objectives of the Study

This study primarily aimed to investigate the potential of Alokon (Broussonetia luzonica) flower extract as a natural antiangiogenic agent. Specifically, it sought to evaluate the antiangiogenic activity of Alokon flower extract using the chorioallantoic membrane (CAM) assay, a cost-effective and reliable model for assessing angiogenesis. The dose-dependent effects of varying concentrations (25%, 50%, 75%, and 100%) of Alokon flower extract on blood vessel formation was determined and its antiangiogenic activity was compared to Quercetin, a known angiogenesis inhibitor, and distilled water as a negative control. In general, this study aimed to establish a scientific basis for using Alokon flower extract in cancer therapy, contributing to advancing plant-based therapeutics. By integrating ethnobotanical knowledge with modern scientific techniques, it bridges traditional practices and contemporary medicine, addressing a significant research gap. The findings align with the United Nations Sustainable Development Goal 3, which promotes good health and well-being, particularly in underserved communities.

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METHODOLOGY

This section outlines the research design, sampling methods, extract preparation process, data collection procedures, and data analysis techniques employed in the study.

Research Design

The study utilized an experimental design, specifically a Completely Randomized Design (CRD), to evaluate the antiangiogenic activity of Alokon (*Broussonetia luzonica*) flower extract. The design included six treatments: a negative control (distilled water), a positive control (Quercetin), and four extract concentrations (25%, 50%, 75%, and 100%). Five replicates were used per treatment, ensuring reliability and validity. This approach provided a quantitative measure of the extract's ability to inhibit blood vessel formation, offering insights into its potential as an affordable and effective alternative for cancer therapy.

Samples

The study used 60 six-day-old fertilized chicken eggs obtained from a supplier in Candon City Public Market, Ilocos Sur. These were selected based on viability as determined by candling, a process that checks the embryo's development before experimentation. Eggs with underdeveloped or non-viable embryos were excluded.

Sampling Technique

The study employed six treatment groups to evaluate the antiangiogenic activity of Alokon (*Broussonetia luzonica*) flower extract using the Chick Chorioallantoic Membrane (CAM) assay. These groups included a negative control (distilled water), a positive control (Quercetin), and four varying concentrations of Alokon flower extract (25%, 50%, 75%, and 100%). Each treatment group consisted of five replicates to ensure reliability and validity in the results. The inclusion of both controls and multiple extract concentrations allowed for a comprehensive assessment of the dose-dependent effects of the Alokon flower extract on blood vessel inhibition.

Preparation of Extract

The concentrations of Alokon flower extract—25%, 50%, 75%, and 100%—were selected to explore its dose-dependent effects on angiogenesis. These concentrations align with findings from previous studies on plant-based extracts, which demonstrated significant biological activity across similar ranges (Hazafa et al., 2020). Preliminary phytochemical screening of the extract revealed a high content of bioactive compounds, such as flavonoids and alkaloids, known for their antiangiogenic properties (Chen et al., 2022). Testing the 100% concentration provided insights into the extract's most potent form, while lower

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concentrations allowed for evaluating its efficacy and determining the potential threshold for activity. This incremental approach ensured a thorough analysis of the extract's effects on angiogenesis.

Data Gathering Procedure

The data gathering procedure for this study involved several systematic steps to ensure the accuracy and reliability of the results. To ensure reproducibility in future studies, the preparation of Alokon flower extract was standardized and meticulously documented. Freshly harvested Alokon flowers were thoroughly cleaned to remove dirt and impurities, then air-dried in a well-ventilated area for five days to prevent degradation of bioactive compounds. The dried flowers were pulverized into a fine powder using a mechanical grinder. A total of 300 g of the powdered sample was soaked in 1500 mL of 95% ethanol for 72 hours with intermittent stirring to ensure thorough extraction. The mixture was then filtered using Whatman No. 1 filter paper, and the filtrate was concentrated using a rotary evaporator at 64°C to remove excess solvent. The resulting crude extract was stored in an airtight container at 4°C until use. For the CAM assay, the extract was diluted with distilled water to achieve the desired concentrations (25%, 50%, 75%, and 100%).

Sixty-six-day-old fertilized chicken eggs, obtained from a local supplier, were candled to ensure viability before incubation at 38 ± 0.2°C and 60–65% humidity for two days. The chorioallantoic membrane (CAM) was prepared by creating an air sac through the removal of 3 mL of albumen and making a window on the eggshell. Treatments were applied dropwise onto 3 mm filter papers, which were then placed on the CAM. Post-treatment, the eggs were sealed with micropore tape to prevent contamination and returned to the incubator for 24 hours. Images of the CAM were captured before and after treatment using a digital single-lens reflex (DSLR) camera, and blood vessel inhibition was analyzed using IKOSA software.

Data Analysis

The collected data were analyzed using descriptive and inferential statistical methods. The mean was computed to determine the average number of blood vessels and their inhibition percentages across treatment groups. Analysis of Variance (ANOVA) was conducted to evaluate significant differences in antiangiogenic activity among the treatments. When significant differences were identified, the Scheffé test was employed as a post hoc analysis to pinpoint specific group differences. The percentage inhibition of blood vessel formation was calculated using the formula:

$$\text{Percent Inhibition} = \frac{X - Y}{X} \times 100 \qquad (1)$$

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Where:

X represents the number of blood vessels before treatment
Y represents the number of blood vessels after treatment.

This analytical framework ensured a comprehensive understanding of the dose-dependent effects of Alokon flower extract and its comparison to controls.

RESULTS AND DISCUSSIONS

Antiangiogenic Activity of Alokon Flower Extract

The antiangiogenic activity of Alokon (*Broussonetia luzonica*) flower extract was assessed through the Chick Chorioallantoic Membrane (CAM) assay, with findings summarized in Tables 1, 2, and 3 and visualized in Figures 1 and 2.

Table 1 presents the percentage inhibition of blood vessel formation for each treatment. Distilled water (T_0), the negative control, showed no angiogenesis inhibition, confirming its inert nature. In contrast, Quercetin (T_1), a well-established angiogenesis inhibitor, achieved the highest inhibition rate of 29.60%, validating its role as the positive control. Alokon extract demonstrated a dose-dependent effect, with its highest concentration (100%) achieving 27.87% inhibition, nearly matching Quercetin. Lower concentrations (25%, 50%, and 75%) showed moderate inhibition, indicating the potential of Alokon extract to inhibit angiogenesis effectively when administered in sufficient concentrations.

These findings align with previous studies on antiangiogenic plant extracts. For instance, Rajasekar et al. (2021) reported a dose-dependent inhibition of angiogenesis using flavonoid-rich extracts from various plants. Similarly, Camposano et al. (2016) demonstrated the antiangiogenic effects of tannin and alkaloid-containing plant extracts, emphasizing their ability to disrupt endothelial cell proliferation and migration. These comparisons suggest that the bioactive compounds in Alokon extract, such as flavonoids, alkaloids, and polyphenols, may operate through similar molecular mechanisms.

The dose dependency observed here reflects the cumulative action of these bioactive compounds. Flavonoids, for example, are known to inhibit VEGF signaling, which is crucial for endothelial cell proliferation and angiogenesis (Herrera & Amor, 2011). This mechanism involves the downregulation of VEGF receptor expression and suppression of downstream pathways like PI3K/AKT and MAPK, which are vital for cell survival and migration (Hazafa et al., 2020). Alkaloids, another significant component, may interfere with hypoxia-inducible factor-1α (HIF-1α), reducing VEGF expression under hypoxic conditions often associated with tumor growth (Cragg, 2005).

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Table 1
Blood Vessel Counts and Percentage Inhibition

Treatment	Pre-treatment Average Count	Post-treatment Average Count	% Inhibition
T_0 - Distilled water	18.0	22.6	0.0%
T_1 - Quercetin	25.0	17.6	29.60%
T_2 – 25% Alokon flower extract	22.4	18.2	18.75%
T_3 - 50% Alokon flower extract	21.8	16.8	22.94%
T_4 - 75% Alokon flower extract	20.6	15.2	26.21%
T_5 - 100% Alokon flower extract	24.4	17.6	27.87%

Figure 1 effectively visualizes the percentage inhibition of angiogenesis across the treatments, highlighting a clear dose-dependent trend. The graph demonstrates a progressive increase in inhibition from 18.75% at 25% concentration to 27.87% at 100%. The highest concentration of Alokon extract performed comparably to Quercetin, underscoring its potential as a natural antiangiogenic agent.

This dose-response relationship is consistent with findings from studies on other plant-derived extracts. For example, Hazafa et al. (2020) reported similar trends in flavonoid-rich plant extracts, attributing the enhanced efficacy at higher concentrations to the cumulative effects of bioactive compounds. These results suggest that Alokon extract's components likely similarly interact with angiogenesis pathways, particularly by targeting VEGF and related signaling cascades.

The ANOVA results in Table 2 confirm significant differences in angiogenesis inhibition among the treatment groups ($p < 0.01$). The large F-value (16.377) indicates that treatment type and concentration had a substantial effect on blood vessel formation. These statistical results validate the observed trends in Table 1 and Figure 1, particularly the efficacy of 100% Alokon extract in achieving inhibition comparable to Quercetin.

The significance of these findings can be attributed to the molecular mechanisms discussed earlier. For instance, polyphenols in Alokon extract may mitigate oxidative stress-induced angiogenesis by neutralizing reactive oxygen species (ROS). This action reduces the activation of proangiogenic factors and promotes endothelial cell apoptosis, thereby disrupting angiogenesis (Chen et al., 2022). The study further corroborates findings by Adelfa et al. (2019) on the efficacy of plant-based extracts in reducing blood vessel formation.

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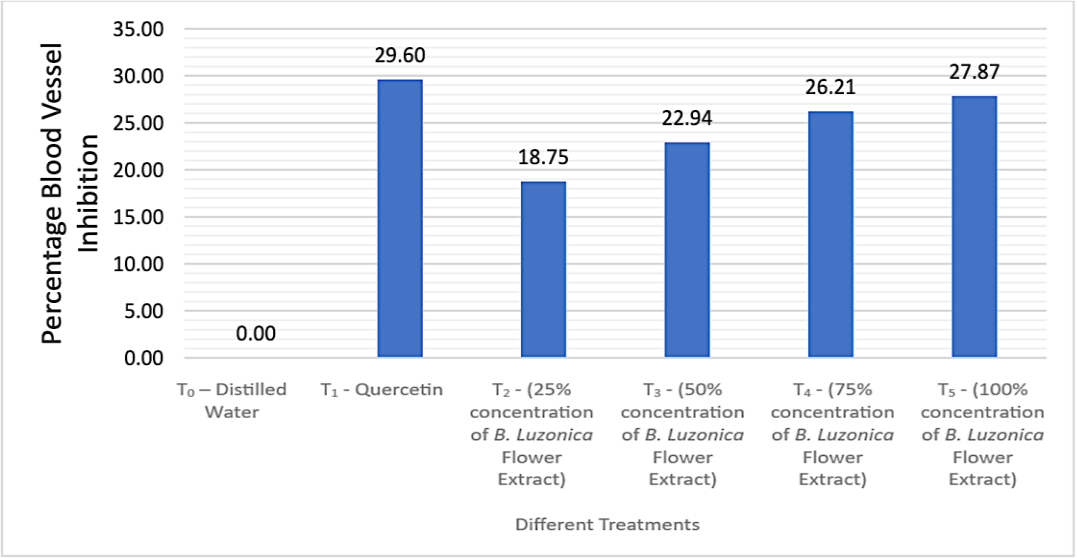
Figure 1

Percentage Inhibition Across Treatments



Significant Difference Between and Among the Antiangiogenic Activity in terms of Blood Vessel Inhibition (Percentage) Using the Different Treatments

Table 2

ANOVA Results on Blood Vessel Inhibition (Percentage)

Source of Variation	Sum of Squares	Df	Mean Square	F	p-value
Between Groups	481.767	5	96.353	16.377	0.000*
Within Groups	141.200	24	5.883		
Total	622.967	29			

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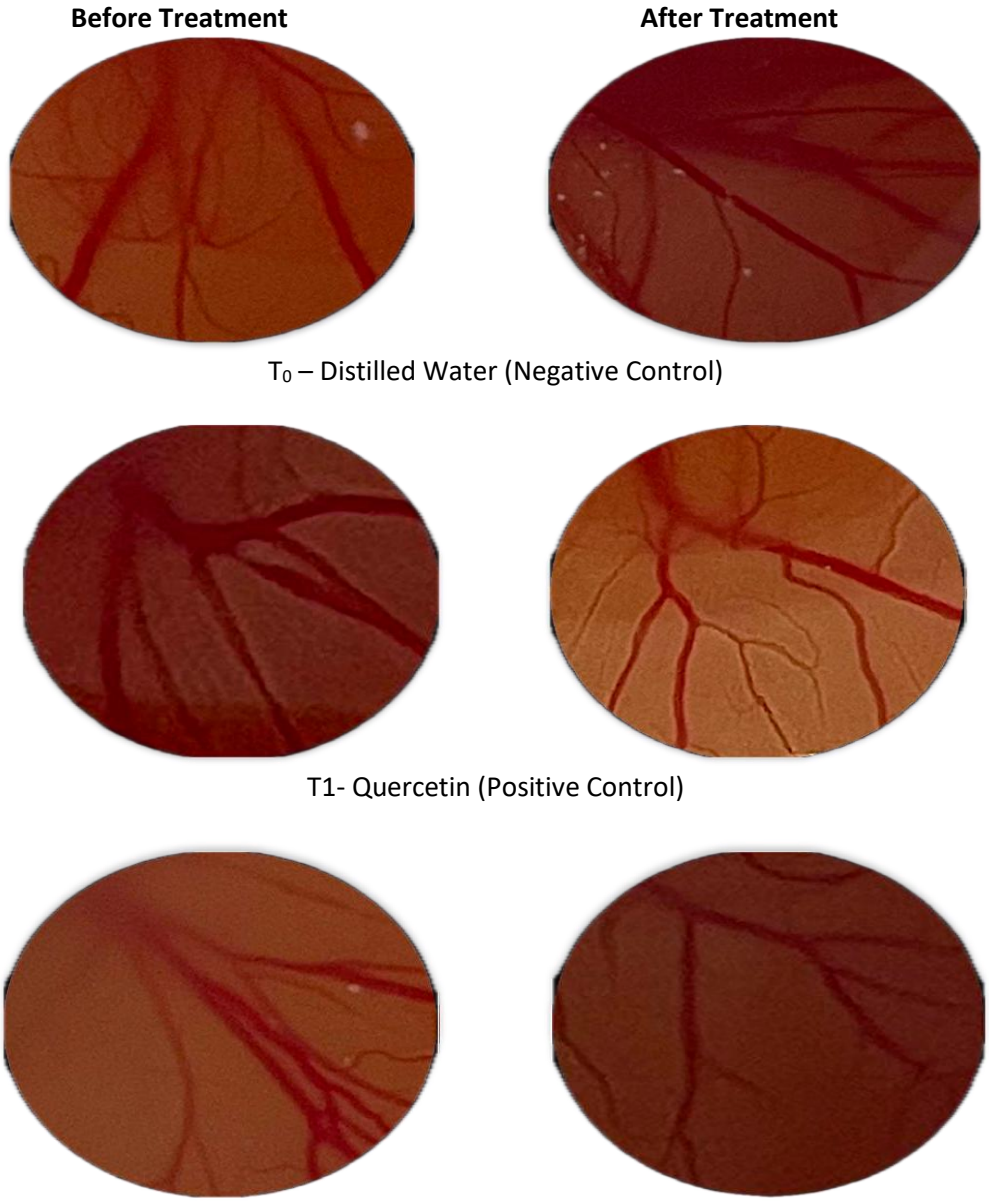
Figure 2

CAM Images Before and After Treatment from IKOSA



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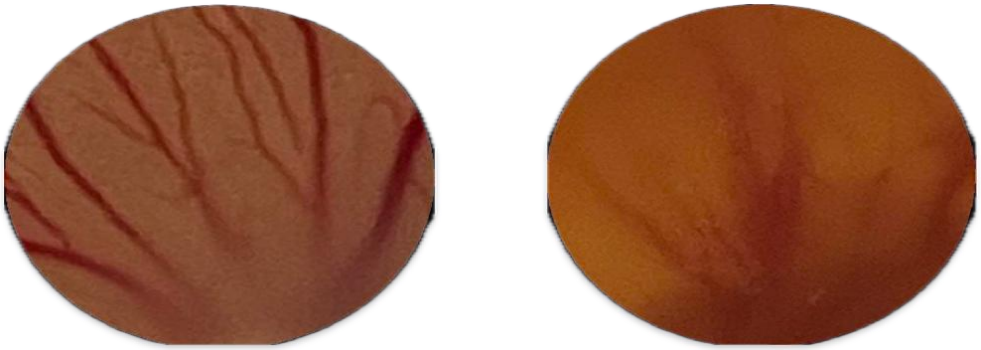
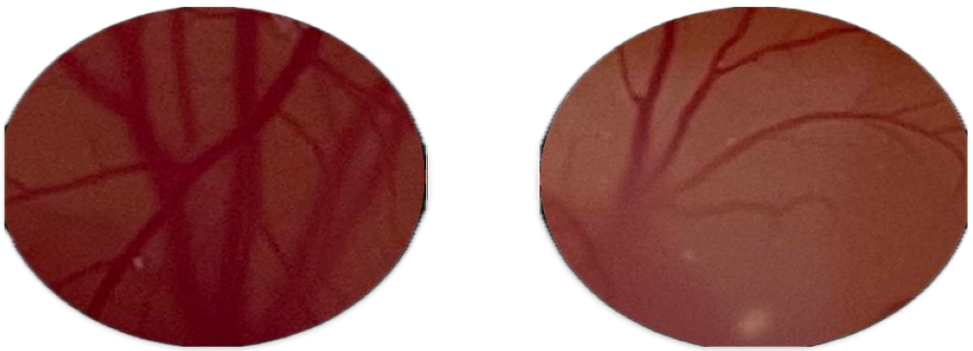
T_3- 50% Alokon Flower Extract



T_4- 75% Alokon Flower Extract



T_5- 100% Alokon Flower Extract

Figure 2 provides visual confirmation of the antiangiogenic effects of the treatments. The CAM treated with 100% Alokon extract shows a significant reduction in blood vessel density compared to the untreated CAM (distilled water), where blood vessels remain dense and interconnected. This visual evidence complements the quantitative data in Tables 1 and 2, reinforcing the conclusion that Alokon extract can inhibit angiogenesis effectively.

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The disruption of blood vessel networks observed here aligns with morphological changes reported in similar CAM assays of antiangiogenic plant extracts studied by Lokman et al., 2012. The reduced vascularization in treated CAMs suggests interference with key molecular pathways, such as VEGF signaling and ROS-mediated angiogenesis, supporting the hypothesized mechanisms of action for Alokon extract.

Scheffe's Test on Significant Difference Between and Among the Antiangiogenic Activity in terms of Blood Vessel Inhibition (Percentage) Using Different Treatments.

Table 3

Scheffe' Test Results for Pairwise Comparisons of Treatments

Comparison	Mean Difference	p-value
T_0 – Distilled Water vs T_1 - Quercetin	12.000	0.000*
T_0 – Distilled Water vs T_2 – 25% Alokon Flower Extract	8.800	0.001*
T_0 – Distilled Water vs T_3 - 50% Alokon Flower Extract	9.600	0.000*
T_0 – Distilled Water vs T_4 - 75% Alokon Flower Extract	10.000	0.000*
T_0 – Distilled Water vs T_5 - 100% Alokon Flower Extract	11.400	0.000*
T_1 – Quercetin vs T_2 – 25% Alokon Flower Extract	3.200	0.515
T_1 – Quercetin vs T_3 – 50% Alokon Flower Extract	2.400	0.781
T_1 – Quercetin vs T_4 – 75% Alokon Flower Extract	2.000	0.844
T_1 – Quercetin vs T_5 – 100% Alokon Flower Extract	0.600	0.999
T_2 – 25% Alokon Flower Extract vs T_3 – 50% Alokon Flower Extract	0.800	0.998
T_2 – 25% Alokon Flower Extract vs T_4 – 75% Alokon Flower Extract	1.200	0.986
T_2 – 25% Alokon Flower Extract vs T_5 – 100% Alokon Flower Extract	2.600	0.719
T_3 – 50% Alokon Flower Extract vs T_4 – 75% Alokon Flower Extract	0.400	0.993
T_3 – 50% Alokon Flower Extract vs T_5 – 100% Alokon Flower Extract	1.800	0.922
T_4 – 75% Alokon Flower Extract vs T_5 – 100% Alokon Flower Extract	1.400	0.972

The Scheffé test reveals significant differences between T_0 (distilled water) and all other treatments, underscoring the antiangiogenic efficacy of both Quercetin and Alokon extract. No significant difference was observed between T_1 (Quercetin) and T_5 (100% Alokon extract), indicating comparable performance.

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These findings suggest that Alokon extract at 100% concentration is as effective as Quercetin, providing a natural and affordable alternative for antiangiogenic therapy. While effective, lower concentrations of Alokon extract require optimization for enhanced performance.

The comparable efficacy of Alokon extract and Quercetin aligns with studies by Chhikara et al. (2022) and Hazafa et al. (2020), which highlight the potential of plant-derived compounds as substitutes for synthetic drugs.

CONCLUSIONS

The study demonstrates that Alokon flower extract (*Broussonetia luzonica*) exhibits antiangiogenic activity comparable to Quercetin, underscoring its potential as a promising natural alternative for cancer therapy. Its accessibility and cost-effectiveness further enhance its appeal as a candidate for future research and development. While these findings highlight the extract's ability to inhibit blood vessel formation, the study acknowledges significant limitations, including the lack of in vivo evaluations, toxicity profiling, and clinical trials, which are essential for validating its safety and therapeutic applicability. Moreover, the broader implications of Alokon as a plant-based therapeutic highlight its potential to support the development of affordable and sustainable cancer treatment options, particularly in resource-limited settings.

RECOMMENDATIONS

The study recommends further exploration of Alokon (*Broussonetia luzonica*) flower extract as a natural antiangiogenic agent. Future research should investigate its potential in combination with other natural compounds, such as Quercetin, to evaluate possible synergistic effects that could enhance efficacy. Optimization of the extraction process by adjusting parameters like solvent type, extraction time, and temperature is essential to improve the bioavailability and potency of the extract. Evaluating the antiangiogenic properties of other plant parts, including the leaves, bark, and roots of Alokon, is also recommended to identify additional therapeutic benefits. Addressing the study's limitations requires conducting in vivo experiments, toxicity profiling, and clinical trials to validate the extract's safety and therapeutic potential. Collaborative efforts with pharmaceutical industries could facilitate large-scale extraction, standardization, and preclinical testing. Community-based cultivation programs should be initiated to make Alokon a cost-effective and accessible cancer care strategy for low-resource settings. Moreover, integrating Alokon with other natural or synthetic agents and studying its potential as part of combination therapies could amplify its therapeutic benefits. Research on interindividual variability in

response to herbal treatments is also advised to identify biomarkers that could guide personalized applications and improve treatment outcomes. Lastly, the dissemination of findings through scientific publications and conferences is crucial to advancing the broader understanding and adoption of plant-based therapies in addressing cancer-related challenges.

ETHICAL STATEMENT

The study strictly adhered to ethical guidelines for research involving animal models. The University Ethics Review Committee approved the use of fertilized chicken eggs in the CAM assay. Fertilized eggs were obtained from a certified supplier, ensuring they met ethical and health standards. Care was taken to minimize harm during the preparation of the CAM, including the use of sterile instruments and precise techniques to create windows on the eggshells and apply treatments. After the experiment, embryos were humanely euthanized by exposure to cold temperatures and disposed of responsibly by burying them at least four feet underground in compliance with environmental and ethical protocols. This process ensured that all procedures were performed with respect for animal welfare and aligned with the principles of the 3Rs—Replacement, Reduction, and Refinement—of animal research ethics.

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REFERENCES

Abdallah, Q., Al-Deeb, I., Bader, A., Hamam, F., Saleh, K., and Abdulmajid, A. (2018). Anti-angiogenic activity of the Middle East medicinal plants of the Lamiaceae family. *Molecular Medicine Reports, 18(2),* 2441-2448. https://www.spandidos-publications.com/mmr/18/2/2441

Adelfa, R., Nioko, A., Gay, S., Cornilla, B., Hernandez, H., Mikaela, R., Macarandang, A., Villena, J., and Magbojos-Magtibay, C. (2020). Wound healing activity of Broussonetia luzonica (Blanco) Bur. (himbabao) leaf extract in ovo duck chorionic allantoic membrane (CAM) assay. *Pacific Journal of Allied Health Sciences*. https://research.lpubatangas.edu.ph/wp content/uploads/2022/06/5-APJAHS-2020-07.pdf

P-ISSN: 0119-3058
E-ISSN: 2945-4093

The Vector: International Journal of Emerging Science, Technology and Management
Volume 33, Issue 1, January - December 2024

Altun, I. & Sonkaya A. (2018) The Most Common Side Effects Experienced by Patients Receiving the First Cycle of Chemotherapy. *Iran J Public Health*. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6123577/

Angio.org Massachusetts. Angiogenesis Foundation. (2018) What is Angiogenesis? http://www.angio.org/about-angiogenesis

Antonio, M., & Vivit, M. (2017). Phytoconstituents and In Vitro Anti-Oxidant Activity Of Selected Indigenous Vegetables In Ilocos. *MMSU Science and Technology Journal*. http://research.mmsu.edu.ph/stjournal/vol7_2_Phytoconstituents.pdf

Arena, R., Guazzi, M., Lianov, L., Whitsel, L., Berra, K., Lavie, C. J., & Shurney, D. (2015). Healthy lifestyle interventions to combat noncommunicable disease. *European Heart Journal, 36 (31)*, 2097–2109. https://academic.oup.com/eurheartj/article-abstract/36/31/2097/2398206

Baclig C. (2023) Philippine Cancer patients lack access to preventive screening. https://www.pids.gov.ph/details/news/in-the-news/ph-cancer-patients-lack-access-to-preventive-screening-costly-treatment

Bandaranayake, W. M. (2006). Quality control, screening, toxicity, and regulation of herbal drugs. *Modern phytomedicine: turning medicinal plants into drugs, 25-57*. https://onlinelibrary.wiley.com/doi/pdf/10.1002/9783527609987#page=45

Bañez, S. E. S. (2022). Ethnobotanical Value of Medicinal Plants Used in the Treatment of Dengue. *The Vector: International Journal of Emerging Science, Technology and Management (IJESTM)*, *31*(1).

Batu, K & De la Merced, L. M. S. (2016). The Radical Scavenging Activity and Effect on Liver Function Enzyme Marker Alanine Aminotransferase of the Flavonoid Extract from the Leaves of Himbabao (*Broussonetia luzonica*) Moraceae. *International Journal of Education Research for Higher Learning, 22(2)*, 1-1. https://www.ejournals.ph/article.php?id=13330

Bhatia, S., Miller, R. C., Haddock, M. G., Donohue, J. H., & Krishnan, S. (2006). Adjuvant therapy for ampullary carcinomas: the Mayo Clinic experience. *International Journal of Radiation Oncology Biology Physics, 66(2),* 514-519. https://www.sciencedirect.com/science/article/pii/S0360301606006894

Bizaba, S. K., Dominguez, E. B., & Kehinde, O. K. (2019). Comparison of antioxidant Activities of the extracts from Hibabao flowers and leaves. *GreenPrints*. https://greenprints.dlshsi.edu.ph/bch/6/

BusinessMirror. (2022). Medicinal Plants in the Philippines and How to Use Them. https://businessmirror.com.ph/2022/06/14/the-importance-of-herbal-medicine/

Calapai, G. (2008). European legislation on herbal medicines: a look into the future Drug safety, 31, 428-431.https://link.springer. com /article /10.2 165 /000 02018

Camposano, J.E., Dela Torre, G.L.T., Laxamana, J.G. & Larcia II, L.L.H. (2016) Screening for the antiangiogenic activity of selected Philippine medicinal plants using chorioallantoic membrane assay. https://doi.org/10.14456/mujps.2016.20

Cancer Research UK. (2020). Cancer Worldwide Statistics. https://www.cancerresearch.uk. org/health-professional/cancer-statistics

Carmeliet, P. & Jain, R. (2000). Angiogenesis in cancer and other diseases. *Nature 407*, 249–257. https://doi.org/10.1038/35025220

Chen Y, Wang L, Liu X, Wang F, An Y, Zhao W, Tian J, Kong D, Zhang W, Xu Y, Ba Y, Zhou H. (2022). The Genus Broussonetia: An Updated Review of Phytochemistry, Pharmacology and Applications. *Molecules. 27(16)*:5344 https://doi.org. /10.33 90/molecules27165344

Chhikara, B. S., & Parang, K. (2022). Global Cancer Statistics 2022: the trends projection analysis. *Chemical Biology Letters, 10(1)*, 451. https://pubs.thesciencein.org/journal /index.php/cbl/article/view/451

Choa, J. B. D., Lu, R. V., Nombrado, M. A., Rayos, G. K. R., Invento, C. D., & Castañeda, G. (2016). Phytochemical screening of Broussonetia luzonicus (Moraceae) leaves. https://www.cabidigitallibrary.org/doi/full/10.5555/20163118

Clemen-Pascual, L. M., Macahig, R. A. S., & Rojas, N. R. L. (2022). Comparative toxicity, phytochemistry, and use of 53 Philippine medicinal plants. *Toxicology Reports*. https://www.sciencedirect.com/science/article/pii/S22147500210

Corpuz, A. V. (2020). Antifungal Effect of Mangosteen (*Garcinia mangostana*) and Pomegranate (*Punica granatum*) Extracts. *The Vector: International Journal of Emerging Science, Technology and Management (IJESTM), 29(1).*

Cragg, G. M., and Newman, D. J. (2005). Biodiversity: A continuing source of novel drug leads. 77(1), 7-24. https://www.degruyter. com/document/doi/10.1351/pac20057

De, L., & Marie, K. (2016). The Radical Scavenging Activity and Effect on Liver Function Enzyme Marker Alanine Aminotransferase of the Flavonoid Extract from the Leaves of Himbabao (*Broussonetia luzonica*) *Moraceae. 22(2),* 1–1. https://ejournals.ph/article.php?id=13330

Department of Agriculture (DA), Bureau of Plant Industry (BPI) (2019). The Himbabao Plant. Philippines. https://iveg.pcaarrd.dost.gov.ph/resource/journal/

Dhara, M., Adhikari, L., and Majumder, R. (2018). Chorioallantoic Membrane (CAM) Assay of Different Extracts of Rhizome and Inflorescence of Heliconia rostrata. *Indian Journal of Pharmaceutical Education and Research, 52(4s),* S246–S251.https://doi.org/10.5530/ijper.52.4s.104

Simbe, D. M. C., Cabrera, L. V. E., Galera, V. N. R., Campul, M. J. R. & Bernal, J. K. S. (2023) Antiangiogenic Activity of Bangkal (Nauclea Orientalis L.) Leaf Extract Using Chorioallantoic Membrane (Cam) In Vivo. University of Northern Philippines.

Domingo, J. C. (2022). Ethnomedicinal Study of Plants in Ilocos Sur. *The Vector: International Journal of Emerging Science, Technology and Management (IJESTM)*, *31(1).*

Egbuna, C., Nadia, S., & Jabeen, N. S. (2018). Pharmacognosy and prehistoric uses of medicinal plants. In Phytochemistry (pp. 3-16). *Apple Academic Press*. https://www.taylorfrancis.com/chapters/edit/10.1201/9780429426193-1/pharmacognosy-prehistoric-uses-medicinal-plants-chukwuebuka-egbuna-sharif-nadia-shaista-jabeen

Ekor, M. (2014). The growing use of herbal medicines: issues relating to adverse reactions and challenges in monitoring safety. *Frontiers in Pharmacology, 4.* https://doi.org/10.3389/fphar.2013.00177

Franelyne Pataueg Casuga, et al., (2016, July). Cytotoxicity of Ethyl Acetate Extract From Broussonetia luzonica (Moraceae) Blanco Leaves against. *ResearchGate*. https://www.researchgate.net/publication/305712013
40

Fu, Y. J., Sun, R., Zu, Y. G., Li, S. M., Liu, W., Efferth, T., and Luo, H. (2009). Simultaneous determination of main taxoids in Taxus needles extracts by solid--phase extraction-high-performance liquid chromatography with pentafluorophenyl column. *Biomedical Chromatography, 23(1)*, 63-70. https://analyticalsciencejournals.onlinelibrary.wiley.com/doi/abs/10.1002/bmc.10

Gamallo, J. P. M., Espere, G., et al., (2016). Evaluation of antiangiogenic property of Ocimum basilica ethanolic leaf extract by using duck embryo chorioallantoic membrane (cam) assay and its morphometric analysis. *Int. J. Herb. Med, 4(4),* 22-26. https://www.researchgate.net/profile/.pdf

Gezici, S., and Şekeroglu, N. (2019). Current perspectives in the application of medicinal plants against cancer: novel therapeutic agents. Anti-Cancer Agents in Medicinal Chemistry (Formerly Current Medicinal Chemistry-Anti-Cancer Agents). https://doi.org/10.2174/1871520619666181224121004

Godofredo U. and Stuart Jr. (2017). Philippine Alternative Medicine. *Himbabao* (Birch Flower) http://www.stuartxchange.com/Himbabao

Graham, L. E., Cook, M. E., and Busse, J. S. (2000). The origin of plants: body plan changes contributing to a major evolutionary radiation. *Proceedings of the National Academy of Sciences.* https://www.pnas.org /doi/ abs/ 10.1073/pnas.97.9.4535

Greenwell, M., and Rahman, P. K. S. M. (2015). Medicinal plants: their use in anticancer treatment. *International journal of pharmaceutical sciences and research, 6(10)*, 4103. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4650206/

Hazafa, A., Rehman, K. U., Jahan, N., & Jabeen, Z. (2020). The role of polyphenol (flavonoids) compounds in the treatment of cancer cells. *Nutrition and cancer, 72(3),* 386-397. https://www.tandfonline.com/doi/abs/10.1080/01635581

Herrera, A. and Amor, E. (2011). Antiangiogenic activity of extracts and fractions from an endemic plant Ardisia pyramidalis using Duck in ovo chorioallantoic membrane assay. *Journal of Medicinal Plants Research*. https://doi. org/10.5897/jmpr

Himbabao, Broussonetia luzonica, Birch Flower: Philippine Medicinal Herbs / Alternative Medicine. (2022). Stuartxchange.com. http://www.stuartxchange.com/Himbabao

Hood, J.D., et al., (2003) Differential alphav-integrin-mediated Ras-ERK signaling during two pathways of angiogenesis. *J Cell Biol; 62*:933–943. https://rupress.org/jcb/article-abstract/162/5/933/33631

Indap, M. A., Radhika, S., Motiwale, L., and Rao, K. V. K. (2006). Quercetin: Antitumor Activity and Pharmacological Manipulations for Increased Therapeutic *Gains. 68(4).* https://search.ebscohost.com/login.aspx?direct=true&profile=ehost

Jadhav, A. D, Gacche, R. N., Shegokar, H. D., Gond, D. S., Yang, Z. (2011). Evaluation of selected flavonoids as antiangiogenic, anticancer, and radical scavenging agents: an experimental and in silico analysis. *Cell biochemistry and biophysics 61*, 651-663. https://link.springer.com/article/10.1007/s12013-011-9251-z

Jaywant, J., Anuya, M., Aruna, K. (2011). Antiangiogenic properties of Boerhaavia diffusa extracts in chick chorioallantoic membrane (CAM). International *Journal of Drug Development and Research. 2011;3(4)*:307-17. 3.42

Kooti W, Servatyari K, Behzadifar M, et al., (2017) Effective Medicinal Plant in Cancer Treatment, Part 2: Review Study. J Evid Based Complementary Altern Med. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5871268/

Lagarde, J. B. B., Laurino, M. Y., San Juan, M. D., Cauyan, J. M. L., Tumulak, M. A. J. R., and Ventura, E. R. (2019). Risk perception and screening behavior of Filipino women at risk for breast cancer: implications for cancer genetic counseling. 10, 281-289. https://link.springer.com/article/10.1007/s12687-018-0391-3

Lokman, N. A., Elder, A. S. F., Ricciardelli, C., and Oehler, M. K. (2012). Chick chorioallantoic membrane (CAM) assay as an in vivo model to study the effect of newly identified molecules on ovarian cancer invasion and metastasis. *International journal of molecular sciences, 13(8)*, 9959–9970. https://doi.org/10.3390/ijms1308

Lydia M. Clemen-Pascual, Rene Angelo S. Macahig, Nina Rosario L. Rojas, (2022). Comparative toxicity, phytochemistry, and use of 53 Philippine medicinal plants, *Toxicology Reports, m Volume 9*, Pages 22-35, ISSN 2214-7500, https://doi.org/10.1016/j.toxrep.2021.12.002.

Luay, M. A. M., Gonzaga, M. F. R., Po, S. K. D., and Arollado, E. C. (2018). Determination of the Antiangiogenic Activity of Telescopium telescopium (horn snail) Extract using in ovo Chorioallantoic Membrane (CAM) Assay. *Acta Medica Philippina, 52(4)*. https://doi.org/10.47895/amp.v52i4.379

Magdadaro, K. B., Artillero, K. J., Lamando, K. L., & Mercurio, A. L. (2023). Angiogenic Effects of Crude Leaf and Flower Extracts of *Cananga odorata* (Ylang-ylang) on Chorioallantoic Membrane of 12 Day Old Duck Embryos. *Ann Biol Res. 14*, 6, 13-16.

Maniago, K. G. N., Mari, C. G. S., Pareja, M. C., Grace, K., and Maniago, N. (2014). Angiogenic effect of Curcuma longa Linn. (turmeric) tea powder on the chorioallantoic membrane of 10-day old Annas luzonica (Duck) eggs. Annals of *Biological Research, 5(4)*, 32-37. https://www.researchgate.net/profile/Marlon-Pareja Biological-Research.pdf

Mann, J. (2002). Natural products in cancer chemotherapy: past, present and future. *Nature Reviews Cancer, 2(2)*, 143-148. https://www.nature.com/articles/nrc723

MMSU Extension Directorate. (2022). Alokon gets highlight in MMSU Techno Sharing. Mariano Marcos State University Extension Directorate; Mariano Marcos State University Extension Directorate. https://extension.mmsu.edu.ph/news/show259/alukon-gets-highlight-in-mmsu-techno-sharing

Morgan, G. W., Foster, K., Healy, B., Opie, C., & Huynh, V. (2018). Improving health and cancer services in low-resource countries to attain the sustainable development goals target 3.4 for noncommunicable diseases. *Journal of global oncology, 4*, 1-11.

Mukherjee, P. K., Kumar, V., Kumar, N. S., and Heinrich, M. (2008). The Ayurvedic medicine Clitoria ternatea—From traditional use to scientific assessment. https://www.sciencedirect.com/science/article/pii/S0378874108004911

Naoyo Nishida, Hirohisa Yano, et al., (2006) Angiogenesis in Cancer, Vascular Health and Risk Management, 2:3, 213-219, DOI: 10.2147/vhrm.s2321344

Nishida, N., Yano, H., Nishida, T., Kamura, T., and Kojiro, M. (2006). *Angiogenesis in cancer. 2(3)*, 213-219. https://www.tandfonline.com /doi/abs/10. 2147/vhrm.s23213

Nissen, N. (2010). Practitioners of Western herbal medicine and their practice in the UK: beginning to sketch the profession. Complementary therapies in clinical practice.https://www.sciencedirect.com/science/article/pii/S1744388110000484

Nowak-Sliwinska, P., Segura, T., and Iruela-Arispe, M. L. (2014). The chicken chorioallantoic membrane model in biology, medicine and bioengineering. *Angiogenesis, 17(4)*, 779–804. https://doi.org/10.1007/s10456-014-9440-7

Othman, Z., Khalep, H. R. H., Abidin, A. Z., Hassan, H., and Fattepur, S. (2019). The Anti-Angiogenic Properties of *Morinda citrifolia*. L (Mengkudu) Leaves using chicken chorioallantoic membrane (CAM) assay. *Pharmacognosy Journal, 11(1)*. http://www.phcogj.com/article/811

Pascual, M. C., Montaño, J. J., Franch, P., Sánchez-Contador, C., and Ramos, M. (2022). Survival of breast cancer by stage, grade and molecular groups in Mallorca, Spain. https://www.mdpi.com/2077-0383/11/19/5708

Paderes, N. M., and Lagangilang, A. P. (2020). Antiangiogenic Activity of Oregano (*Origanum vulgare*) Aqueous Extract In-Vivo Through Chick Chorioallantoic Membrane (Cam) *Assay. Syst. Rev. Pharm, 11*, 12221227.https://www.academia.edu/download/99527369/antiangiogenic-activity-of-oregano-origanum-vulgare-aqueous-extract-invivo-through-chick-chorioallantoic-membrane-cam-as.pdf

Peteros, N. P., and Uy, M. M. (2010). Antioxidant and cytotoxic activities and phytochemical screening of four Philippine medicinal plants. Journal of Medicinal Plants Research, 4(5), http://www.academicjournals.org/JMPR

Philippine Bureau of Plant Industry (2019) https://www.buplant.da.gov.ph/

Qureshi, H., Anwar, T., Khan, S., Fatimah, H., and Waseem, M. (2020). Phytochemical constituents of Broussonetia papyrifera (L.) L'He'r. ex-Vent: http://indianchemicalsocietycom/portal/uploads/journal/D2020_01_7_Extended_1580346196.pdf

Rajasekar, N., Sivanantham, A., Ravikumar, V., & Rajasekaran, S. (2021). An overview on the role of plant-derived tannins for the treatment of lung cancer. https://www.sciencedirect.com/science/article/pii/S0031942221001485

Rao S., and Suresh C. (2013). In vitro and in vivo effects of the leaf extracts of Cassia tora and Cassia sophera in reducing the cytotoxicity and angiogenesis. https://www.cabidigitallibrary.org/doi/full/10.5555/20133320817

Ribatti, D., Vacca, A., Roncali, L., and Dammacco, F. (2000). The chick embryo chorioallantoic membrane as a model for in vivo research on anti-angiogenesis. 1(1), 73-82. https://europepmc.org/article/med/9032025

Ruma M., Madhumita, R., Kunnumakkara, A. B., Apurba, S., Sutapa, M., and Jaydip, B. (2015). Repair activity impaired by arsenic: recovery by phytochemicals. *International Journal of Current Microbiology and Applied Sciences*. https://www.cabdirect.org/globalhealth/abstract/20153129858

Sagmayao K., Rabago K., Sibayan K., Tolentino J.,Ventura A., and Segismundo A. (2021) Antiangiogenic Activity Of Narra Tree (Pterocarpus Indicus) Bark Extract In Chick Chorioallantoic Membrane In Vivo. University of Northern Philippines

Saxena, M., Saxena, J., Nema, R., Singh, D., and Gupta, A. (2013). Phytochemistry of medicinal plants. *Journal of pharmacognosy and phytochemistry, 1(6),* 168-182.46. https://www.phytojournal.com/archives?year=2013&vol=1&issue=6&part=A

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Smith, R. A., Cokkinides, V., and Brawley, O. W. (2009). Cancer screening in the United States, 2009: a review of current American Cancer Society guidelines and issues in cancer screening. *CA: a cancer journal for clinicians, 59(1)*, 27-41. https://acsjournals.onlinelibrary.wiley.com/doi/abs/10.3322/caac.20008

Su, B., Zhong, P., Xuan, Y., Xie, J., Wu, Y., Chen, C., and Zheng, X. (2023). Changing Patterns in Cancer Mortality from 1987 to 2020 in China. *Cancers, 15(2)*, 476. https://www.mdpi.com/2066518

Tsai, Y. T., Cheng, P. C., & Pan, T. M. (2012). The immunomodulatory effects of lactic acid bacteria for improving immune functions and benefits. *Applied microbiology and biotechnology.* https://link.springer.com/article/10.1007/s00253-012-4407-3

Tugume, P., & Nyakoojo, C. (2019). Ethno-pharmacological survey of herbal remedies used in the treatment of pediatric diseases in Buhunga parish, Rukungiri District, Uganda. https://link.springer.com/article/10.1186/s12906-019-2763-6

UP Media and Public Relations Office. (2022). UP expanding the PGH to serve more Filipinos. *University of the Philippines*. https://up.edu.ph/up-expanding-the-pgh-to-serve-more-filipinos/

World Health Organization. (2022). Cancer. *World Health Organization*. https://www.who.int/news-room/fact-sheets/detail/cancer