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EFFECTIVENESS OF ANNONA MURICATA (SOURSOP) ON VARIOUS TYPES OF CANCER: A SYSTEMATIC REVIEW

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ABSTRACT:

Annona muricata has long been used as a cancer treatment herb; it is also known by the names graviola, soursop, and guanabana. *A. muricata*'s mode of action and effectiveness in the treatment of cancer have been well examined. This systematic review set out to compile the body of research on the variables associated with *A. muricata* extract's anticancer properties. Methods: The studies included were in-vitro, preclinical animal, and human studies written in English. Studies assessing *A. muricata* extract and its anticancer activity on a variety of deadly cancers were searched in PubMed, Elsevier Science Direct, Wiley Online Library, Ovid Medline, Cochrane, Ovid Medline, and Prospero databases between the start of the study and June 2022. The findings suggest that *A. muricata* and its constituents have anticancer effects. However, the amount and length of time used in research on animals to illustrate toxic effects might not be promptly applicable to human effects. The current review's overall conclusion suggests that *A. muricata* has a favourable anticancer profile. Future research into its use in people with a variety of cancers is required.

KEYWORDS: *Annona muricata,* anticancer agent, soursop, graviola, herbal treatment, natural anticancer therapy.

INTRODUCTION

Cancer disease is one of the leading causes for mortality in the entire globe. The Agency for Cancer Research Internationally (IARC) estimates that 17.0 million new cases of cancer will be reported in 2018. Population aging and population growth are expected to increase the global cancer burden to 27 million new cases and 16 million cancer deaths by 2040. Lung, liver, stomach, colorectal, prostate, breast, and cervical/uterine cancers are probably the most frequently diagnosed cancers in economically developing countries. The most common cases of cancer in 2020 were:

- breast (two million cases);
- lung (two million cases);
- colon and rectum (nearly two million cases);
- prostate (one million cases);
- skin (non-melanoma) (one million cases);
- stomach (nearly one million cases).[1]

The continuous increase in the number of cancer cases raises concerns about the effectiveness of the various treatments available. As a consequence, patients are looking for conventional therapies for cancer such as radiation therapy, surgery, and chemotherapy treatment. Medicinal plants are widely recognized as the foundation of preventive medicine and therapeutic practices. A combination of several treatments such as chemotherapy, surgery, radiotherapy, immunotherapy and photodynamic therapy are often used to treat cancer. Yet, if cancer therapy impacts ordinary cell metabolism, such may result in significant adverse reactions. As a result, at small doses, herbal remedies may be applied as a complementary drug without causing adverse reactions or preventing the anti-apoptotic method [2].

Annona muricata (*A. muricata*) is a plant which is traditionally employed as a cancer prevention agent. It is additionally referred to as soursop, graviola, and other names. *Annona muricata*, a member of the Annonaceae family, is well-known for its medicinal properties. The *Annona muricata* plant is native to America, but it has since become naturalized, is grown in tropical climates, and is eaten by people, mostly for the treatment of cancer and parasite illnesses. Cough, fever, pain, and skin conditions are all treated with the plant. It is also used as an insecticide, pesticide, vermifuge, antispasmodic, astringent, anticancer, sedative, and antihypertensive. Soursop plants have been shown to exhibit a variety of chemical compositions in their roots, bark, leaves, fruit flesh, and seeds [3]. The plant's bark and root are frequently used to treat worm infestations, diarrhoea, and dysentery. Fever can also be treated with the fruit flesh. Fruit that hasn't been peeled is used as an astrigen to cure scurvy and intestinal atony.

In India, plant leaves, roots, and bark are all utilized as antihelminth agents, while the flesh and flowers are used to treat cataracts. In addition, using soursop leaves as a cancer treatment is

safer and more hopeful than using radiation or chemotherapy. In preclinical animal model systems and in vitro culture, soursop has shown having therapeutic effects against a variety of tumours and disease agents. These benefits are usually evaluated for their capacity to target the disease precisely, with little to no impact on normal cell viability. [4]

A. muricata (soursop) extract is one of countless botanical products that have shown promising medicinal value. More than 212 components of phytochemicals have been documented in soursop extracts made from several plant sections. The particular bioactive components in charge of the several types of soursop have significant anticancer, antioxidant, anti-inflammatory, antibacterial, and other health effects of it includes alkaloids, flavonoids, sterols, annotaceous acetogenins (metabolites and products of the polyketide pathway). Compounds derived from *A.muricata* have been linked to a variety of anti-cancer effects, including cytotoxicity & apoptosis induction, necrosis & proliferation inhibition on breast and prostate cancer cell lines, colorectal cancer, lung cancer, leukaemia, kidney disease, pancreatic, liver, oral, melanoma, cervical, and other cancers. More rigorous studies, however, are required to establish safe and effective care regimens. This review summarizes recent advances in the application and mechanisms of *A. muricata* extracts in vitro and in vivo against several cancer[4]. Soursop leaf treatment for cancer is also more effective and less hazardous than treatment with chemotherapy or ionizing radiation

A. muricata solvent extracts and their anticancer activities are tabulated below:

Extract (solvent)	**Cancers (cell lines)**
n-Hexane	Cervical (HeLa) cancer
Chloroform	Cervical (HeLa) cancer
Pentane	Melanoma (A375) cancer
n-Butanolic	Melanoma (MDA-MB-435S) cancer
DMSO	Pancreatic (Capan-1, FG/COLO357, and CD18/HPAF) cancer
Fungal strain	Breast (MCF-7) colorectal (HTC-8) lung cancer (A549)

	hepatic (Bel-7402) gastric (BGC-823) ovarian (A2780) cancers
H_2O	Squamous cell carcinoma (SCC-25) melanoma (A375) prostate (PC-3) pancreatic (CD18/HPAF) breast cancer
Hexane	Breast (MCF-7 and MDA-MB-231) colorectal (HT-29 and HCT-116) lung cancer (A549) leukemic (U-937) pancreatic (Capan-1) hepatic (Hep G2) cancers
Ethyl acetate	Breast (MCF-7 and MDA-MB-231) colorectal (HT-29 and HCT-116) lung (A549) leukemic (U-937) hepatic (Hep G2) cervical (HeLa) cancers

MATERIALS AND METHODS:

STUDY DESIGN:

A systematic review of clinical studies was conducted in order to figure out the implications of *Annona muricata* extracts on the cancer therapies for various types of the same.

SEARCH STRATERGY:

The online databases were used to locate previously published works on *Annona muricata* and its effects on various types of cancer.

INCLUSION CRITERIA:

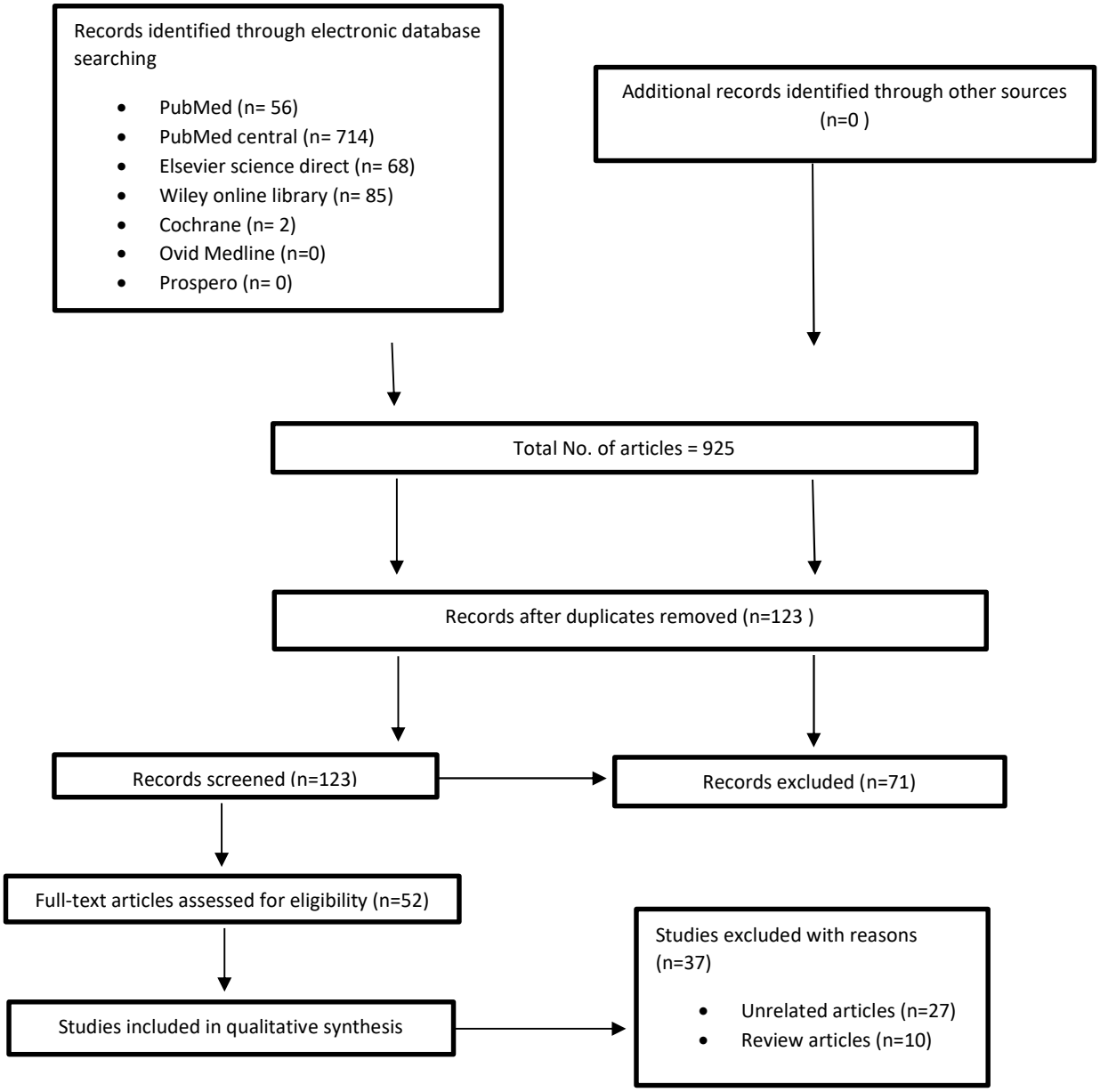
1. Studies published in English
2. Full-text articles
3. Publications over the years
4. Animal Studies
5. Human studies
6. In-vitro studies
7. In-vivo studies

EXCLUSION CRITERIA:

1. Articles published in languages other than English
2. Simply abstracts available.
3. Unrelated content

SEARCH ENGIENE:

- PubMed
- Elsevier science direct
- Wiley online library
- Ovid Medline
- Cochrane
- Ovid Medline
- Prospero



The flow diagram in Figure 1 depicts how several studies were found, examined, evaluated for being eligible, excluded, and added to the systematic review.

925 articles were identified in digital databases after conducting a search using suitable match terms. After removing duplicates, 123 articles were screened, and 52 full-text articles were available, 15 of which were included in the qualitative synthesis.

TABLE1: CHARACTERISTICS OF THE INCLUDED STUDY IN THE SYSTEMATIC REVIEW

S.NO	AUTHOR NAME	YEAR	LOCATION	TYPE OF CANCER	DESIGN	SAMPLE	TECHNIQUE
1.	Maya Tejasri et al[3]	4 June 2018	Indonesia	Liver cancer	In vitro-TUNEL method	For cell culture, SF-1603 extracted from *A.muricata* leaf, Hep G2 cell line, penicillin, streptomycin, and trypsin were used.	Apoptosis was detected utilizing TUNEL method. In the mathematical analyses, a regression model was used.
2.	Akhmad Endang Zainal Hasan et al[5]	21 June 2022	Indonesia	Cervical HeLa cancer	In vitro MTT assay method	10 samples of *A.muricata* leaf extract, malt glucose yeast peptone broth, MTT indicator	The inhibitory concentration 50 (IC50) value was determined for five isolated fungi based on the greatest inhibition in one concentration.
3.	Minarni et al[6]	20 June 2017	Indonesia	Breast cancer	In vitro MTT assay method	12 extracts of *A.muricata* leaf endophytic fungi	The MTT assay technique was used to determine the toxicity of fungi samples contrary to MCF-7 (Michigan

							Cancer Foundation-7) cells in vitro. At a concentration of 100 g/mL, four of the twelve isolates demonstrated significant effectiveness against the growth of cancer cells. Following that, the four isolates were chosen for further IC50 determination, which included evaluating the inhibition of cancer cell proliferation at extract concentrations of 25, 50, 100, 200, and 400 g/mL.
4.	Miranti Kania Dewi et al[7]	30 December 2021	Indonesia	Breast cancer	In vitro MTT assay method of MCF_7 & $T_{47}D$ of	7 *A.muricata* leaf aqueous extracts (SLAE) + 7 Doxorubicin	The test was performed at the following concentrations of soursop leaf aqueous extracts (SLAE): 250

					breast cancer culture		g/mL, 125 g/mL, 62.5 g/mL, 31.25 g/mL, and 15.625 g/mL, 7.8125 g/mL, and 3.906 g/mL, respectively. Whereas Doxorubicin was administered in 100-g increments. Both SLAE and doxorubicin have 1/8 IC50. Cell . An ELISA reader was used to determine viability.
5.	Murdani Abdullah et al[8]	9 April 2017	Indonesia	Colorectal cancer	In vitro MTT assay method	6 samples - ESFAM, EIFAM, ORAC, 5FU, Leucovorin & FULV	In a 96-well plate, cells were seeded. The media was replaced with ORAC extract once it reached the confluence.
6.	Ade Arsianti et al[9]	11October 2019	Indonesia	Cervical HeLa cancer	In vitro MTT	8 various concentrations with various	The extracts were divided into eight concentrations

					assay method	polarities of *A.muricata* leaf	. The cytotoxicity of A.muricata leaves samples contrary to HeLa cervical cancer cell lines was examined via the MTT assay, and the value of the IC50 was calculated.
7.	Damien Mikael Hansra et al[10]	5 May 2014	USA	Breast cancer	Ex vivo Human subject	A chart review of one patient diagnosed with BC between 1999 and 2012. A sixty six year-old women cancer survivor used to boil ten to twelve dry *A.muricata* leaves in water for 5-7 minutes, then take 8 oz PO daily.	A detailed clinical history was obtained, including the patient's age at diagnosis, stage at diagnosis, treatment (chemotherapy, hormone therapy, soursop), and response to therapy. A review of laboratory data, including liver function testing and tumor markers, was carried out. Finally, imaging with

							FDG PET CT was examined from diagnosis to study conclusion.
8.	Syed Najmuddin et al[11]	24 August 2016	Malaysia	Breast cancer	In vivo mice subject	19 AMCE samples	**The MTT assay was used to screen on breast cancer cell lines (MCF-7, MDA-MB-231, and 4 T1) 19 specimens of *Annona muricata* in multiple places. Following tumor inclusion, the mice were fed the extract.**
9.	Lili Indrawati et al[12]	2017	Indonesia	Colorectal cancer	Ex vivo Human subject	Thirty colorectal cancer outpatients who had undergone primary tumor resection were enrolled in a randomized double-blind placebo-controlled	The cytotoxicity of serum from both groups of patients was tested against colorectal cancer cell lines.

						pre-post-trial. That they were divided to two categories: 1 group got *A. muricata* leaf extract (14) and the other got a placebo (14) for eight weeks. The trial included 28 subjects allocated uniformly between the two groups.	
10.	Yuri N. Clement et al[13]	21 October 2016	Trinidad	Prostate cancer, breast cancer, colorectal cancer	Ex vivo Human subject	150 patients Breast (n = 88) Prostate (n = 36) Colorectal (n = 25) ingested *A.muricata* leaves and fruits	An interviewer-administered, evaluated new questionnaire was used to execute a descriptive, cross-sectional survey at a couple of treatment centers on the island.
11.	Teressa Rojas	22 October 2016	France	Liver cancer	Ex vivo Human subject	88 patients used	A comparative behavioral epidemiological survey was

	Rojas et al[14]					*Annona muricata*	carried out among liver cancer patients at Peru's National Cancer Institute. To collect information, personal interviews were carried out via a questionnaire that was semi-structured.
12.	George Awuku Asare et al[15]	18 November 2014	Bangladesh	Prostate gland cancer	In vivo mice subject	For two months, twenty F344 male mice (200 g) were injected with 30 mg/mL (ten mice) and 300 mg/mL (ten mice) and fed ad libitum together with 10 mice that served as controls.	*A muricata* aqueous leaf extract was used in the MTT assay on BPH-1 cells. Cells were subjected to stimulation with 0.5, 1.0, and 1.5 mg/mL extract for 24, 48, and 72 hours. As potential target genes, Bax and Bcl-2 were investigated. 20 F344 male mice (200 g) were injected with 30

							mg/mL (10 mice) and 300 mg/mL (10 mice) before being fed ad libitum with 10 mice serving as controls.
13.	Okolie Ngozi Paulinus et al[16]	26 July 2013	Nigeria	Colorectal cancer	In vivo mice subject	Doses in vivo: 250 or 500 mg/kg into male Sprague-Dawley rats	The male wistar rats were divided into seven groups. They were fed mashed potatoes with cycas leaf powder. ELAM was given to the patient. Following sacrifice, a colon section was dissected for biochemical analysis.
14.	María P. Torres et al[17]	01 October 2013	USA	Pancreatic cancer	In vivo mice subject	Doses: 10–200 µg/mL, IC50 = 73 µg/mL in vitro. 50 mg/kg/35 days injected orthotopically in the	The PC cells FG/COLO357 and CD18/HPAF were incubated with various concentrations of Soursop

						pancreas of athymic nude mice	extract for 48 hours.
15.	Sulaiman Hamizah et al[18]	June 2012	Malaysia	Skin cancer	In vivo mice subject	180 6-7 a week old ICR-treated mice were treated with topically applied 7,12 - dimethylben za anthracene (DMBA 100ug/100ul acetone) followed by 10 weeks of advancemen t with croton oil (1% in acetone/ two times a week).	In six to seven a week old ICR mice provided just one topical application of 7,12-dimethylbenza anthracene (DMBA 100ug/100ul acetone) and advancement by successive applications of croton oil (1% in acetone/ twice a week) for a period of ten weeks, AMLE was tested for chemopreventi ve effects. The incidence, burden, and volume of morphological tumors were calculated, and skin tissue was histologically examined.

Table 1 displays the intervention traits in the studies that were included. *Annona muricata* and its efficacy against various types of cancer were reviewed and compared in all of the preceding studies.

TABLE 2: THE RESULTS DATA FROM PROVIDED RESEARCH

S.NO	AUTHOR NAME	YEAR	LOCATION	CONCLUSION	RESULT
1.	Maya Tejasri et al[3]	4 June 2018	Indonesia	It was concluded that the new *A.muricata* leaves active compound (SF-1603) is a potent anticancer agent with the ability to induce apoptosis in HepG2 cell line culture, and thus it can be used as a candidate for new HCC therapy agents.	The novel A.muricata leaves activate compound SF-1603, which induces apoptosis in cancerous liver cell types..
2.	Akhmad Endang Zainal Hasan et al[5]	21 June 2022	Indonesia	Endophytic fungi extracts from *A.muricata* leaves are toxic to cervical cancer cells, as evidenced by inhibition of HeLa cancer cell proliferation in vitro. Sir-SM2 is extremely harmful to the cervical cancer cells while being harmless to Chang's normal cells.	The crude ethyl acetate extract of Sir-SM2 endophytic fungi showed high cytotoxicity to cervical cancer cells (HeLa cells) but was less toxic to normal Chang cells; thus, it may be a natural anticancer agent.
3.	Minarni et al[6]	20 June 2017	Indonesia	Endophytic fungi isolated from *A.muricata* leaves have a chance to be utilized as cancer prevention agents.	With an IC50 of 19.20g/ml, Sir G5 possessed the greatest activity against cancer.

4.	Miranti Kania Dewi et al[7]	30 December 2021	Indonesia	The anticancer properties of *A.muricata* leaf aqueous extract are insufficient contrary to MCF7 and T47D breast cancer cultured cell lines, and a mixture of *A.muricata* leaf aqueous extract compounds and doxorubicin has an antagonistic effect on MCF7 and T47D breast cancer cells.	In T47 breast cancer culture, the IC50 for *Annona muricata* leaf aqueous extract was 84g/ml, and in MCF7, it was 166.5g/ml.
5.	Murdani Abdullah et al[8]	9 April 2017	Indonesia	Caspase-3 activity was higher in *Annona muricata* leaf extract than in leucovorin and placebo. The results of this study indicate *Annona muricata* extract of leaves may have anticancer effects through raising caspase-3 activity, a proapoptotic marker.	The findings suggest that *Annona muricata* leaf extract has anticancer properties by increasing caspase-3, a pro-apoptotic marker.
6.	Ade Arsianti et al[9]	11October 2019	Indonesia	*A.muricata* extracts from leaves have an opportunity to be established into a novel alternative treatment for cervical carcinoma.	**3 *A.muricata* extracts had high cytotoxicity in contrary to HeLa cells. Etanol extract had the highest cytotoxic activity, with an IC50 of 35.51 g/mL, followed by ethyl acetate (IC50: 5.91 g/mL) and hexane**

					(IC50: 8.39 g/mL).
7.	Damien Mikael Hansra et al[10]	5 May 2014	USA	Before this plant-derived extract can be used in those with breast cancer, additional clinical study is needed to determine its effectiveness, effective dosage, possible interactions with other drugs, and toxicity.	Tumor markers at the time of *A.muricata* and Xeloda initiation were CEA 12.5 ng/ml (0.0 - 3.4 ng/mL), CA 15-3 1249.0 U/ml (0.0 - 25.0 U/mL), CA 27-29 1295 U/ml, and CEA 2.9, CA 27-29 32 U/ml, and CA 15-3 20.7 U/ml in 2007. For over 5 years, the patient's disease was stable, with no side effects from therapy.
8.	Syed Najmuddin et al[11]	24 August 2016	Malaysia	The findings indicate that B1 AMCE is an intriguing possibility for treatment of cancer, particularly in breast cancer, and that it merits further research as a substitute to traditional drugs, while additionally emphasizing the importance of *A.muricata* sample selection when evaluating the drug's	The chosen B1 AMCE reduced tumour size and weight, demonstrated anti-metastatic properties, and induced T1 cell apoptosis.

				potential medicinal impact on cancer.	
9.	Lili Indrawati et al[12]	2017	Indonesia	More research is required to figure out the cumulative impact of *A.muricata* leaf extract, especially its cytotoxic activity against cells with colorectal cancer and the state of nutrition.	Ex vivo and clinical studies revealed that the supplemented group had higher cytotoxicity than the placebo group.
10.	Yuri N. Clement et al[13]	21 October 2016	Trinidad	The results of this study discovered a number of commonly used natural remedies and nutritional foods among breast, prostate, and colon cancer survivors in Trinidad. Although functional foods are rarely a problem, herbs may react with traditional treatment such as chemotherapy, and doctors must warn patients about the potential of herb-drug relations.	Various *Annona muricata* L. extracts demonstrated anti-proliferative effects in vitro via apoptosis and arrest of the cell cycle in the prostate, the colon, and carcinoma of the breast cell lines in 121 (80.7%) of 150 patients.
11.	Teressa Rojas Rojas et al[14]	22 October 2016	France	The findings confirm that Herbal Medicines are still an important primary health care resource in Peru, even for serious diseases like liver cancer.	According to the findings, 14% of Peruvian patients with liver cancer used *A. muricata* in the form of herbal medicine to

					treat cancer-related symptoms.
12.	George Awuku Asare et al[15]	18 November 2014	Bangladesh	*Annona muricata* reduces prostate size and inhibits BPH-1 cell proliferation, possibly through apoptosis.	After forty-eight hours, the best outcomes were achieved, with cells nearly disappearance at seventy-two hours. The test groups' prostates were smaller, and there was less prostatic secretion, as well as flattening of the acinar epithelial lining. *Annona muricata* inhibits BPH-1 cell proliferation and shrinks prostate size, possibly through apoptosis.
13.	Okolie Ngozi Paulinus et al[16]	26 July 2013	Nigeria	The findings suggest that *Annona muricata* has a promising future in the treatment of colorectal cancer.	The ELAM and cycas groups had no glandular hyperplasia, mucosal erosion, or oedema, according to the findings. These findings support ELAM's protective role in biochemical events associated with colorectal cancer.

14.	María P. Torres et al[17]	01 October 2013	USA	In vitro experiments revealed that the natural extract's compounds inhibited several pathways involved in PC cell proliferation and metabolism at the same time. Such inhibitors reduced tumour growth and metastasis in orthotopically transplanted pancreatic tumour-bearing mice.	The results show that the natural product reduces tumorigenicity and metastasis in orthotopically implanted pancreatic tumors, indicating promising properties against pancreatic cancer.
15.	Sulaiman Hamizah et al[18]	June 2012	Malaysia	It is assumed that *A. muricata* acts similarly because it increased the average latency period of tumour occurrence by 10-20%, thereby prolonging the promotional stage by delaying tumour formation and decreasing the number of tumors in mouse skin when compared to the carcinogen-treated control.	Even at low doses, the *A.muricata* leaves extract was able to suppress tumour initiation and progression.

Table 2 displays the findings and outcomes of *Annona muricata* and its beneficial effects on various types of cancer in the aforementioned studies. The end result and findings of the aforementioned studies were favorable, indicating *Annona muricata* (soursop) to be a promising candidate for cancer treatment.

TABLE 3: BIAS ASSESSMENT AS INCLUDED IN THE STUDIES

AUTHOR NAME	RANDOM SEQUENCE	ALLOCATION CONCEALMENT	BLINDING OF PARTICIPANTS	BLINDING OF PERSONNEL	BLINDING OF OUTCOME	INCOMPLETE OUTCO	SELECTIVE REPORTING

	GENERATION				ASSESMENT	ME DATA	
Lili Indrawati et al[12] 2017	+	+	+	+	+	+	+

Table 3 shows the bias analysis of all the research above. It is categorized as high-risk bias "-", low-risk bias "+" and unclear "?"

AUTHOR NAME	Syed Najmuddin et al[11] 2016	George Awuku Asare et al[15] 2014	Okolie Ngozi Paulinus et al[16] 2013	María P. Torres et al[17] 2013	Sulaiman Hamizah et al[18] 2012
RANDOMIZATION	?	?	+	?	+
ALLOCATION CONCEALMENT	+	+	+	+	+
COMPARISON GROUP	N/A	N/A	N/A	N/A	N/A
CONFOUNDING AND MODIFYING VARIABLES	N/A	N/A	N/A	N/A	N/A
IDENTICAL STUDY GROUPS	+	+	+	+	+
BLINDING OF PERSONELL AND PARTICIPANTS	+	+	+	+	+
INCOMPLETE OUTCOME DATA	+	+	+	+	+
EXPOSURE CHARECTERIZATION	+	+	+	+	+

OUTCOME ASSESSMENT	+	+	+	+	+
MEASURED OUTCOME REPORT	+	+	+	+	+
OTHER POTENTIAL THREATS	N/A	N/A	N/A	N/A	N/A

+= Low risk of bias; -= high risk of bias; ?= unclear risks of bias; N/A= Not Applicable

DISCUSSION:

There is always a constant requirement to develop affordable and easily available anticancer drug with minimum side effects. Hence, this review points the effect of *Annona muricata* also known as Graviola's effect on different types of cancers.

According to WHO, breast cancer (BC) is a highly prevalent cancer in women and accounted for the majority of malignancy in 2020. Treatment of BC remains difficult due to toxicity and drug resistance in current therapies. This article presents the case of soursop demonstrating clinical benefit in a a 66-year-old female diagnosed with BC[11]. Despite receiving single-agent treatment with chemotherapy, the mean survival with no progression on Xeloda in a tumours developing is just a handful of months. Anonaceous acetogenins, the primary active ingredient of soursop, are long chain fatty acid products that are highly toxic to tumour cells, such as resistant to many drugs forms of cancer cells. Soursop was found to inhibit tumorgenicity and metastasis in pancreatic cancer cells. Toxically, soursop is capable of causing seizures and myeloneuropathy, with signs resembling Parkinson's condition. There were no major adverse reactions for the patient. Damien Mikael Hansra et al. [10] conclude with a call for additional studies to assess the performance, efficient dose, possible interactions with other drugs, and toxic effects of this plant-based collect so that it can be approved for consumption by breast cancer patients.

Soursop (*Annona muricata* L.) was the more frequently utilized medicinal product and useful food, as reported by Yuri N. Clement et al[13], with 80.7% using its bark, leaves, seeds, and the fruits on an ongoing basis. The most frequently consumed natural treatments and nutritional supplements among breast, prostate, and colon cancer sufferers in Trinidad have been determined in this questionnaire.

The MTT technique was applied on three types of breast cancer cells in Syed Najmuddin et al's[11] study to figure out the effectiveness (IC50) of 19 samples of *Annona muricata* from different parts of the world Following that, an in vivo anti-cancer study was carried out in which mice were fed extract after tumour induction. The chosen B1 AMCE decreased cancer weight and size, displayed

anti-metastatic characteristics, and caused apoptosis in 4 T1 cells in vitro and in vivo cells. The findings indicate where B1 AMCE is a declaring treatment for cancer, especially with breast cancer.

The toxicity of fungal extracts against MCF-7 (Michigan Cancer Foundation-7) cells in vitro was determined using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay method in Minarni et al[6] study. The findings demonstrated that the extracts had no effect on regular growing cells. Endophytic fungus isolated from soursop leaf might possess anticancer properties.

Miranti Kania Dewi et al[7] examine the anticancer properties of soursop leaf aquoxes extract and the integrated impact of a drug called doxorubicin on MCF7 alongside T47D breast carcinoma cells. The Laboratory of Universitas Gadjah Mada, carried out an unbiased in vitro experiment in the month of August 2018 of MCF7 and T47D breast tumour culture cells research. In contrast, the sum of the test demonstrated that aqueous extract of soursop leaf was anti-doxorubicin for both T47D and MCF7 tumour cell cultures.

Cancer of the colon is becoming more prevalent in Asia, during which it is currently among the most prevalent tumours [12] in addition to lung cancer. The aim of this was to assess the effects of *A. muricata* leaf extract on humans. Experimental and clinical investigations of patient serum stated greater cytotoxicity in the enriched group with respect to the placebo group. Lili Indrawati et al[12] research concludes with a requirement of further research to investigate the cumulative impact of *A.muricata* leaf extract, especially on criteria closely linked to its cytotoxic capacity regarding colon cancer cells and state of nutrition.

Okolie Ngozi Paulinus et al[16] conducted a study where, seven groups of male Wistar rats were formed. They were given mashed potatoes flavoured with cycas leaf powder. They were given Ethanolic Leaf extracts of *A.Muricata*. After the sacrifice, a section of the colon was dissected for biochemical analysis. *Annona muricata*, based to the outcomes, has an upward trajectory in the management of cancer in the colon.

According to the findings, neither the ELAM nor the cycas groups had glandular hyperplasia, mucosal erosion, or oedema. These findings support ELAM's protective role in colorectal cancer biochemical events.

Murdani Abdullah et al[8] used caspase-3, a cell apoptotic marker, to investigate the apoptosis-inducing impact of soursop (*Annona muricata*) extract of leaves on the colon cancer cell line COLO-205. Cell cultures were incubated with 10 g/ml soursop leaf and then compared to those incubated with 10 g/ml leucovorin as a positive control and placebo as a negative control. *A. muricata's* extract of leaves raised caspase-3 by 1.09 times in contrast to pure cell line. In the COLO-205 carcinoma of the colon cell line, it possessed higher concentrations of caspase-3 instead of leucovorin and placebo. These findings could imply that *Annona muricata* leaf extract has anticancer properties by increasing caspase-3 activity, a proapoptotic marker.

Cancer of the prostate is an extremely prevalent tumours and the second leading cause of mortality of cancer in men. In 2012, the prostate was responsible for approximately 29% of all new cancer cases and 9% of all cancer deaths in the United States [15]. The MTT test was conducted out on BPH-1 cells via aqueous leaf extract of *A.muricata*. Cell development and the shape have been investigated under the microscope. A total of 20 F344 male mice were injected with 30 mg/mL (10 mice) and 300 mg/mL (10 mice) and fed ad libitum with 10 control mice. The mice had to be sacrificed after sixty days of life. The prostate gland, the seminal vesicles and the testicles were histologically investigated. *Annona muricata* inhibited cell proliferation with an IC50 of 1.36 mg/ml. The most favourable outcomes appeared after a period of 48 hours, with cells almost the demise at 72 hours. The Bax gene was upregulated, while the Bcl-2 gene was downregulated. This article concludes that *Annona muricata* inhibits BPH-1 cell proliferation and shrinks prostate size, possibly through apoptosis [15].

Skin cancer is perhaps the most prevalent form of cancer, contributing to 30% of the total number of cancers diagnoses globally [18]. The anti-cancer properties of an ethanolic product of *A. muricata* leaves (AMLE) (100ug/100ul acetone) and promotion by twice-weekly treatment with croton oil (1% in acetone) were evaluated in six to seven weeks aged ICR mouse strains that were provided just one topical injection of 7,12-dimethylbenzanthracene (DMBA). Morphological tumour incidence, burden, and volume were calculated, and skin histology was examined.[19] At concentrations of 100 and 300 mg/kg, AMLE entirely halted cancer growth at all stages of development. A histopathological examination revealed that tumour growth in the AMLE-treated groups exhibited only minor hyperplasia and the absence of keratin pearls and rete ridges. The findings imply that the *A.muricata* leaves extract can also inhibit tumour initiation even at low doses.

Conventional chemotherapies are ineffective against Pancreatic tumours. The main reason for PC patients' poor prognosis is the disease's insidious and sporadic nature, which frequently presents with no specific early clinical symptoms. The cytotoxicity, cell metabolism, cancer-associated protein/gene expression, tumorigenicity, and metastatic properties of PC cells were evaluated using an extract from the tropical tree *Annona muricata*. Maria P Torres et al[17] research revealed that Soursop caused PC cell necrosis by inhibiting cellular metabolism.

Another deadliest type of cancer is liver cancer. With 745000 deaths per year [14]. A comparative behavioural epidemiological survey was performed on 4,444 liver cancer patients attending the National Cancer Institute of Peru [14]. In-person interviews took place via an informal survey. The use of Herbal Medicines in liver cancer patients in Peru has been reported, primarily in relation to general consumption before the onset of disease and second, after the onset of symptoms that the patient will associate with their tumour. In parallel, 4,444 overall Herbal Medicine consumption in people without cancer were evaluated for comparison. The correspondence evaluation was utilized to discover possible associations between signs of cancer and herbal treatment use. The survey included 88 cancer patients and 117 noncancerous people.

Overall, 68.3% of those polled said they used Herbal Medicines on a regular basis to maintain their general health. These findings confirm that Herbal Medicines is still one of Peru's primary health care resources, even for serious diseases like liver cancer.

In Maya Tejasri et al[3] study, HepG2 cell lines cultured in DMEM/F12 were used. A total of 3 interference groups, all of which had a different SF-1603 concentration. According to the findings, the unaffected group had less cells that were apoptotic than the ones receiving therapy groups. The apoptotic impact was dependent on dose reflected by a significant positive relationship (r=0.847) within cell death rate and SF-1603 concentration. According to the findings, the novel soursop leaves active compound SF-1603 has a strong ability to induce apoptosis on liver cancer cell line culture, and thus can be used as a candidate for new agent for liver cancer therapy.

Cancer of the cervix is the 4th largest cause for mortality in women with cancer [5]. Cancer therapies involve surgery, hormonal therapy, chemotherapy, radiation therapy, targeted treatment with drugs, and vaccinations (American Cancer Society, 2016). Inevitably, a few of these procedures may result in loss of hair, premature menopause, tiredness, sickness, mouth as well as throat sores, and issues with memory (Mehta and Bhargava, 2019). Herbal remedies and plant chemicals derivatives, on the contrary present, are medicinal. Endophytic fungi derived from extracts from soursop leaves impeded the proliferation of HeLa tumour cells within in vitro, illustrating toxicity against cervical tumour cells.[20] The crude ethyl acetate extract of Sir-SM2 endophytic fungus revealed a significant cytotoxicity to cells with cervical cancer (HeLa cells) but had been not as harmful to typical Chang cells, implying that it could serve as a naturally occurring anticancer agent. According to shape, these isolated Sir-SM2 endophytic fungal species are related to the Penicillium genus, and molecular confirmation using the Internal Transcribed Spacer demonstrates high resemblance with Penicillium crustosum[5].

The leaves of *A.muricata* were crushed and soaked in three solvents that are of varying polarity: ethanol , ethyl acetate, and hexane. Following that, the extracts were diluted into 8 different concentrations. The MTT technique was utilized to evaluate the toxicity of *A.muricata* leaf extract sample in contrary to cervical tumour cells in HeLa, and the IC50 value was estimated[9]. The 3 *A.muricata* extracts have been shown to be extremely toxic to cervical HeLa cells. *A.muricata* plant leaves have a chance to be established into an innovative replacement treatment for cancer of the cervical cavity.

Therefore, it is apparent that *Annona muricata* extracts has a potential effect anticancer effect that can manage deadliest cancers like **breast cancer, colorectal cancer, prostate cancer, skin cancer, pancreatic cancer, liver cancer and also cervical cancer.**

CONCLUSION:

Despite advances in synthetic smaller molecule-based aimed anticancer treatments with better outcomes for patients, cancer stays one of the biggest causes of death globally due to difficulties such as higher toxicities and drug susceptibility. Natural remedies derived from

medicinal plants keep enormous potential in the management of cancer. By exploring into *Annona muricata*'s biologically active chemical molecules in addition to both in vitro and in vivo studies that were conducted to clarify the molecular pathways that govern the activity of these components, this assessment shows *Annona muricata*'s potential for cancer prevention and other health-related reward. Soursop is not just a desired tropical tree plant which serves as a vital basis for food processing and a substitute conventional medicine, but it also includes a plethora of phytochemicals with a broad spectrum of biochemical activities, including cancer prevention, an antioxidant and other characteristics that are not restricted to the ones addressed within.

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