GSC Biological and Pharmaceutical Sciences
eISSN: 2581-3250 CODEN (USA): GBPSC2
Cross Ref DOI: 10.30574/gscbps
Journal homepage: https://gsconlinepress.com/journals/gscbps/

(REVIEW ARTICLE)

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Therapeutic Potential of *Annona muricata* Leaves Extract in Targeting Cervical Cancer: A Systematic Review

Icha Nadhirotul Izza Afida [1,*] and Savira Oktavia Ainiyati [2]

[1] *Department of Histology and Pathology Anatomy, Faculty of Medicine, University of Jember, Jember, East Java, Indonesia.*
[2] *Department of Microbiology, Faculty of Medicine, University of Jember, Jember, East Java, Indonesia.*

GSC Biological and Pharmaceutical Sciences, 2025, 33(02), 013–024

Publication history: Received on 16 September 2025; revised on 30 October 2025; accepted on 01 November 2025

Article DOI: https://doi.org/10.30574/gscbps.2025.33.2.0425

Abstract

Cervical cancer, the second most common cancer among women worldwide, is caused almost entirely by human papillomavirus (HPV). Considering the limitations of existing cervical cancer therapies, there is a need for treatments that can maximize therapeutic efficacy while minimizing side effects. *Annona muricata* Lin., or soursop, a member of the Annonaceae family, has a long history of use in traditional medicine for cancer treatment. The aim of this study is to provide a comprehensive understanding of the therapeutic potential of *Annona muricata* leaves in targeting cervical cancer. This study employs a systematic literature review based on the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) guidelines. The literature was searched from five databases: Google Scholar, PubMed, ProQuest, ScienceDirect, and Springer. A total of 6 articles met the eligibility criteria. It was included in the final analysis. A. *muricata* demonstrates cytotoxic activity, induces apoptosis, upregulates p53 gene expression, and downregulates anti-apoptotic genes. Biactive components in A. *muricata,* such as acteogenins and stigmasterol, play a crucial role in these mechanisms through mitochondrial pathway activation and reactive oxygen species modulation. Overall, the evidence suggests that *A. muricata* leaves possess promising therapeutic potential as a natural anticancer agent for cervical cancer.

Keywords: *Annona muricata* leaves; Cervical cancer; Cervical carcinoma; Phytochemical; Soursop leaves

1. Introduction

Cervical cancer remains highly prevalent in countries with low Human Development Index (HDI) levels. Globally, cervical cancer is the second most common cancer in terms of both incidence and mortality among women of reproductive age. (1). Persistent chronic human papillomavirus (HPV) infection is the primary cause of cervical cancer. (2). HPV strains 16 and 18 account for approximately 71% of cases, followed by strains 58, 33, 45, 31, and 52 (1,3). Cervical cancer's natural history, which includes HPV infection, precancerous growth, and malignant invasion, is well understood. Many cases of cervical cancer were caused by a combination of other risk factors, such as smoking, HIV infection, early initiation of sexual activity, oral hormonal contraception, and having multiple sexual partners. Because of all these factors, cervical cancer is a disease that may be substantially avoided (1). In Indonesia, cervical cancer continues to be the most prevalent gynecological cancer, accounting for the second-highest patient count after breast cancer. The incidence of cervical cancer in Indonesian women is roughly 36,633 instances (9.2% of new cancer cases in both sexes and all ages), with a mortality rate of 21,003 cases (9%), according to the GLOBOCAN 2020 data (3,4).

There have been many therapies for cervical cancer, such as surgery, chemotherapy, radiotherapy, and many others. Surgical intervention remains the primary treatment for early-stage cervical cancer, focusing on complete tumor removal while preserving organ function and vital nerves whenever possible (5). This decision is multidisciplinary, considering factors such as fertility preservation, general health, and menopausal status (6). In advanced disease stages

* Corresponding author: Icha Nadhirotul Izza Afida

or when surgical intervention is not feasible, radiochemotherapy (RCT) is the primary treatment modality. This approach employs advanced technologies such as intensity-modulated radiotherapy and MRI-guided brachytherapy to ensure precise radiation delivery, commonly combined with cisplatin as a radiosensitizing agent. However, clinicians must carefully consider the high morbidity of adjuvant RCT (7). Other treatments, including drug combinations like cisplatin/topotecan or cisplatin/paclitaxel with bevacizumab, have shown benefits in survival rates, and carboplatin can be used as an alternative to lessen side effects (8). Immunotherapy is also promising due to the tumor's viral etiology and high immunogenicity. The clinical application of this therapy remains constrained by several challenges, including tumor resistance, treatment-related toxicity, patient specificity, and substantial financial costs (9).

Considering the limitations of existing cervical cancer therapies, there is a need for treatments that can maximize therapeutic efficacy while minimizing side effects. Natural products represent a promising alternative. The diverse active compounds found in herbal plants are hoped to enhance the effectiveness of treatment and reduce the side effects that occur during therapy. Extensive research has been conducted on various plant species, their phytochemical constituents, and the medicinal properties of their compounds (10). One such plant is *Annona muricata* Lin., or soursop, a member of the Annonaceae family with over 130 genera and 2,300 species. This plant, which grows in tropical and subtropical regions like Southeast Asia, South America, and African rainforests, contains various pharmacologically active compounds. The plant produces edible fruit year-round and has a long history of use in traditional medicine to treat conditions such as skin diseases, respiratory illnesses, fever, bacterial infections, diabetes, hypertension, and even cancer (11).

The primary active compounds found in *Annona muricata* such as acetogenins, alkaloids, and flavonoids. Subsequent analyses of the *Annona muricata* leaf extract revealed the presence of diverse secondary metabolites, comprising flavonoids, terpenoids, saponins, coumarins, lactones, anthraquinones, glycosides, tannins, and phytosterols (12). Given the numerous active compounds, this review aims to provide a comprehensive understanding of the therapeutic potential of *Annona muricata* leaves in targeting cervical cancer.

2. Materials and methods

This study employs a systematic literature review as its research method. The data for this research were gathered from existing online studies (secondary data). The literature was sourced from five databases: Google Scholar, PubMed, ProQuest, ScienceDirect, and Springer. The search utilized a combination of keywords, including "*Annona muricata leaves*", "cervical cancer", "cervical carcinoma", "phytochemical", "soursop leaves"and connected by the Boolean operators "OR" and "AND".

The inclusion criteria used in this systematic review was (a) article published between 2015-2025; (b) research conducted in any country; (c) publications written in English; (d) studies available in full-text and open-access format; (e) indexed in Scopus (Q1-Q4); (f) original research articles; (g) study that investigate soursop leaves (*Annona muricata)* as a potential anticancer agent against cervical cancer. While the exclusion criteria used in this study were (a) review articles; (b) studies without full-text access; (c) articles not relevant to the topic of interest.

The literature screening and eligibility assessment process for this review followed by the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) guidelines. The procedure involved the following stages: (1) defining the review topic; (2) formulating the research question; (3) Identifying relevant keywords; (4) Establishing inclusion and exclusion criteria; (5) Conducting database searches using the selected keywords; (6) Screening studies based on titles, abstract and keywords; (7) Retrieving full-text articles relevant to the topic; and (8) synthesizing the eligible studies.

3. Results and discussion

A total of 6 articles were identified as meeting the predefined eligibility criteria and were subsequently included in the final analysis. These articles were selected following a systematic search across five electronic databases, which initially yielded many records. After removing duplicates and applying the inclusion and exclusion criteria, only studies directly addressing the anticancer potential of *Annona muricata* against cervical cancer remained eligible. The study identification, screening, and selection process is presented in the PRISMA flowchart (Figure 1), which provides a transparent overview of how the final pool of articles was determined. To facilitate comparison and synthesis, the essential characteristics of the included studies—such as author, year of publication, country of origin, study design, and key findings—are summarized in Table 1. These characteristics are further examined and discussed in detail within

the discussion section, where each study's strengths, limitations, and relevance to the research objective are critically analyzed.

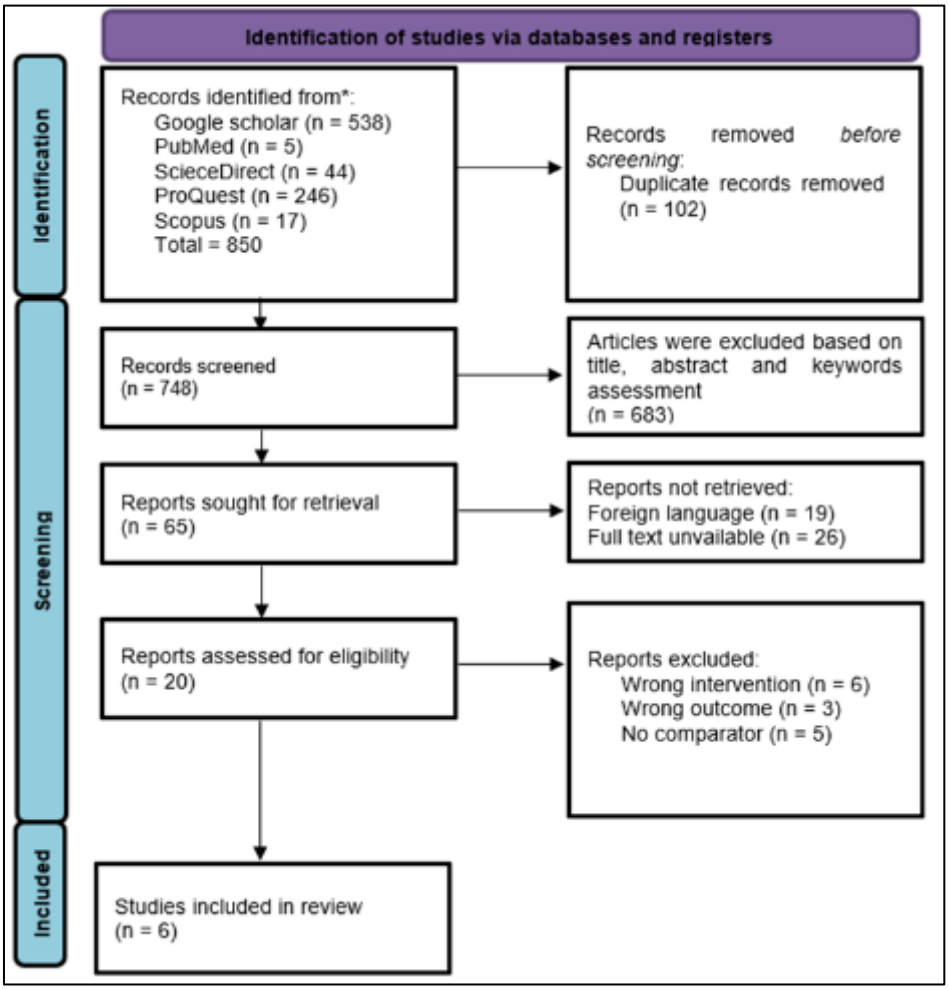

Figure 1 PRISMA Diagram of Article Search Process

Table 1 Characteristics of the included study

Author, Year	Study Design	Population / Subject	Intervention	Methods/Assays	Comparator	Outcomes
Qorina et al., 2020 (13)	In vitro	HeLa cells	*Annona muricata* leaf extract using solvents: ethanol (polar), ethyl acetate (semi-polar), hexane (non-polar)	Maceration extraction MTT assay for cytotoxicity IC_{50} determination	Positive control using cisplatin Negative control using untreated cells	All extracts showed cytotoxicity against HELa cells (IC_{50} ethanol = 5,91 µg/ml; IC_{50} ethyl acetate = 7,56 µg/ml; IC_{50} hexane = 8,39 µg/ml). Cisplatin IC_{50} ethanol = 1,78 µg/ml.

Gavamukulya et al., 2021 (14)	In vitro	HeLa cells PC3 cells PNT1A cells	Silver nanoparticles synthesized from ethanolic extracts of *Annona muricata* fruits (AgNPs-F) and leaves (AgNPs-L)	Resazurin cytotoxicity assay Migration (wound healing assay) Clonogenic assay qRT-PCR for CASP9, CXCL1, CXCR2	Positive control using 5-Fluorouracil (5FU) Negative control using vehicle DMSO	Cytotoxicity: IC_{50} HeLa: AgNPs-F = 38.58 µg/mL, AgNPs-L = 57.63 µg/mL, 5FU = 10.38 µg/mL. Selectivity index: AgNPs-F = 7.8 (highest, safer for normal cells), AgNPs-L = 2.36, 5FU = 3.56. Migration: AgNPs-F inhibited wound closure in HeLa cells (anti-metastatic). Clonogenic assay: AgNPs-F = 0% recovery in HeLa (permanent effect), 40.81% recovery in normal PNT1A cells (low toxicity). Gene expression: Upregulation of CASP9, downregulation of CXCL1/CXCR2 axis (pro-apoptotic, anti-metastatic mechanism).
Astirin et al., 2021 (15)	In vitro	HELA cells	Nanoparticles from the chloroform fraction of *Annona muricata* leaves (nano-SL) and the ethyl acetate fraction of *Caesalpinia sappan* wood (nano-SW),	Nanoparticle synthesis via chitosan-NaTPP ionic gelation Characterization (particle size, zeta potential, transmittance) Cytotoxicity (MTT assay) Apoptosis/necrosis detection via	Positive control using Cisplatin Negative control using Untreated cells	IC_{50} values: nano-SL = 63.32 µg/mL, nano-SW = 40.88 µg/mL, Cisplatin = 56.93 µg/mL. Synergism: Combined dose (1/8 IC_{50} each) → CI = 0.13 (strong

			tested individually and in combination	flowcytometry (Annexin V/PI), CXCL1, CXCR2		synergistic effect). Cell death: nano-SL induced 36.5% apoptosis + 42.6% necrosis; nano-SW induced 14% apoptosis + 18% necrosis; combined dose increased apoptosis 1.5–2× control.
Ahamed et al., 2022 (16)	In vitro and in silico	HeLa cells Vero cells	Isolated stigmasterol (STML) from the ethanolic extract of *Annona muricata* Linn leaves	Sohlet extraction Cytotoxicity assay (MTT) Thin Layer Chromatography (TLC) Antioxidant assays (DPPH, ABTS) Anti-inflammatory assay (albumin denaturation) Spectral analysis (UV-Vis, FTIR, DFT computations) Docking against VHR phosphatase (PDB ID: 3F81)	Ascorbic acid (antioxidant)	Antioxidant activity: IC_{50} STML 13,41 µg/ml; IC_{50} absorbic acid 14,73 µg/ml Cytotoxicity: HeLa IC_{50} = 11,58 µg/ml; Vero IC_{50} = 173,8 µg/ml In silico binding energy -6.6 kcal/mol; Ki = 14,34 µM.
Astirin et al., 2023 (17)	In vitro	HeLa cells	Fractions, isolates, and nanoparticles from soursop (*Annona muricata*) leaves (chloroform fraction) and sappan wood (*Caesalpinia sappan*) (ethyl acetate fraction)	Extraction & fractionation (chloroform for soursop, ethyl acetate for sappan); Column chromatography; TLC Nanoparticle formulation via chitosan–NaTPP ionic gelation Characterization (particle size, zeta potential, SEM, FTIR) Cytotoxicity (MTT assay) Apoptosis/necrosis (flow cytometry)	No explicit positive control drug was mentioned; comparisons were made across fractions, isolates, nanoparticles, and their combinations	Cytotoxicity (IC_{50}): Soursop fraction = 7.13 µg/mL, isolate = 8.17 µg/mL, nanoparticles = 88.98 µg/mL; Sappan fraction = 13.07 µg/mL, isolate = 6.9 µg/mL, nanoparticles = 82.53 µg/mL. Cell death: all forms induced apoptosis and necrosis; isolates were most potent. Synergy: nanoparticle combination at

						1/10 IC_{50} gave combination index (CI) = 0.54 (synergistic). Antioxidant activity: IC_{50} STML 13,41 µg/ml; IC_{50} DPPH 14,73 µg/ml.
Mariappan et al., 2025 (18)	In vitro	C33A (HPV-) ME180 (HPV+)	Folate–chitosan nanoparticles (FACSNPs) loaded with acetogenins (epomuricenin -A, -B, epomusenin-B) isolated from *Annona muricata* leaves	Extraction with petroleum ether Isolation via chromatography; Structural ID (NMR, MS, IR, UV) Nanoparticle synthesis (ionotropic gelation, folic acid conjugation) Characterization (FTIR, zeta potential, SEM, TEM, TGA) MTT cytotoxicity assay Scratch wound healing assay Cellular uptake/internalization (fluorescent imaging)	Negative control using untreated cells (vehicle)	Cytotoxicity: AMPE I (epomuricenin -A) IC_{50} = 14.8 µg/mL (C33A), 16 µg/mL (ME180). FACSNPs IC_{50} = 45.3 µg/mL (C33A), 62.7 µg/mL (ME180). CSNPs IC_{50} = 98.2 µg/mL (C33A), 125.6 µg/mL (ME180). Mechanism: FACSNPs showed better uptake via folate receptor-mediated endocytosis, and were more cytotoxic to C33A than ME180. Migration assay: 20 µg/mL FACSNPs inhibited wound closure at 24 h (anti-metastatic effect).

3.1. Taxonomy and botanical view of *Annona muricata*

Annona muricata (*A. muricata*) is commonly known by various names, including soursop, graviola, guanabana, and durian belanda (19). This plant belongs to the Annonaceae family. *A. muricata* is a small, evergreen tree. The genus name for Annona may have come from the Latin word "anon," which means "yearly produce." It is 5 to 10 meters high and 15 to 83 centimeters in diameter, with low branches. When crushed, the dark-green leaves release a strong odor (20). It has low branches and measures 5 to 10 m in height and 15 to 83 cm in diameter. The dark-green leaves have a pungent smell when crushed. The unique-scented hermaphrodite flowers are usually produced individually or in small clusters

on aged wood. The flowering phase begins between the ages of three and four, though this might vary depending on the environment. The fruit may be round or heart-shaped, depending on the pollination method. The skin contains several tiny, recurved spines that are 0.5–1.3 cm apart (21).

The taxonomic position of *Annona muricata* is as follows, according to the Integrated Taxonomic Information System (2025) (22):

Kingdom : Plantae

Division : Tracheophyta

Class : Magnoliopsida

Order : Magnoliales

Family : Annonaceae

Genus : Annona L.

Spesies : *Annona muricata* L.

Figure 1 (A) *Annona muricata* tree; (B) leaves; (C) flowers; and (D) fruits (23)

3.2. Potential Anticancer Effects of *Annona muricata* Against Cervical Cancer

Various illnesses, including dermatitis, diarrhea, dysentery, fever, hypertension, diabetes, and cancer, can be treated using an extract from *A. muricata*. According to earlier studies, extract from A. *muricata* leaves was shown to activate the apoptotic process and induce sustained homeostasis in Raji cells by increasing p53 gene expression and decreasing hsp70 expression (24). To determine the most effective solvent against cervical cancer, Qorina et al. used a variety of solvents. Hexane, ethanol, and ethyl acetate are the solvents used in this study. The cytotoxicity of *A. muricata* against HeLa cells used to treat cervical cancer was examined using the MTT test. The outcome shows that the concentration of the extract and the percentage of inhibition are positively correlated (13). The MTT assay is a widely utilized method for assessing cytotoxicity. In viable cells, MTT transforms the yellow tetrazolium salt into purple formazan crystals that may be quantified with a spectrophotometer (25).

The IC_{50} number, which indicates the concentration required for the extract to inhibit 50% of the cancer cells' activity, is another way this study calculates the extract's cytotoxicity. A lower IC_{50} value indicates a higher cytotoxic potency of the extract against cancer cells. When tested against HeLa cervical cancer cells, the ethanol extract of *A. muricata* exhibited the highest cytotoxicity (5.91 µg/mL), followed by ethyl acetate (7.56 µg/mL) and hexane (8.39 µg/mL). When compared to Cisplatin as a positive control, the IC_{50} value of these three extracts remained higher (IC50 value = 1.78 µg/mL) (13). Cisplatin (CP), a widely used chemotherapeutic agent, is known for its potential to cause significant damage to normal healthy cells. CP also causes direct damage to the mitochondrial DNA, which leads to oxidative stress, by raising the intracellular ROS level (26). The oxidative stress caused by CP is non-selective, which damages normal tissues and increases toxicity in malignancies. CP, including myelosuppression, hepatotoxicity, nephrotoxicity, and immunotoxicity, brings on numerous adverse consequences. Combination therapy with natural products may be a new way to combat CP-induced side effects because these side effects can make chemotherapy less effective (27,28).

The biological components of *A. muricata* may have an impact on its anticancer properties. According to research, it originates from a unique substance known as annonaceous acetogenin that belongs to the group Annonaceae. This molecule is derived from C32 or C34 long-chain fatty acids. This molecule's cytotoxicity mechanism involves blocking

complex I in the mitochondria and lowering ATP synthesis in the cytoplasm, which disrupts oxidative phosphorylation and triggers the apoptotic process. Due to their continuous proliferation, cancer cells exhibit a higher demand for ATP than normal cells. Consequently, they are more susceptible to the cytotoxic effects of annonaceous acetogenins than healthy cells. However, anonaceous acetogenin is a polar molecule that dissolves more readily in polar solvents. This may help to explain the findings of the study, which indicated that, in comparison to other extracts, the ethanol extract with the highest polarity has the most cytotoxicity (13,29).

Mariappan et al. (18) also investigated *A. muricata*-based nanoparticles incorporating acetogenins, bioactive substances in *A. muricata*. Acetogenins have strong cytotoxic and antitumor effects on a range of cancer cells. They also act as potent inhibitors of mitochondrial complex I (NADH: ubiquinone oxidoreductase) by blocking the electron transport chain. Three acetogenins—AMPE I, AMPE II, and AMPE III—were isolated from the leaves of *A. muricata*. The AMPE II and AMPE III have lower cytotoxicity. At the same time, AMPE I was more active and superior in terms of cytotoxicity, exhibiting IC_{50} values of 14.8 µg/mL and 16 µg/mL against C33A (human cervical squamous cell carcinoma with HPV-negative) and ME180 (human cervical squamous cell carcinoma with HPV-positive) cells. Fluorescence is also used to analyze the potential of the mitochondrial membrane (18)As demonstrated by fluorescence experiments, the observed depolarization of the mitochondrial membrane implies that acetogenins directly compromise mitochondrial integrity, which is consistent with earlier findings about their mode of action (30).

Acetogenins' stability, solubility, and intracellular delivery are probably improved by their encapsulation in nanoparticle form, which raises their cytotoxic potency (31). Additionally, nanocarrier systems offer selective targeting, decreased degradation, and regulated release, all of which are beneficial for lowering systemic toxicity and raising the therapeutic index (32).

The presence of NPs (Nanoparticles) within the cells due to folate receptor endocytosis is indicated by the strong red fluorescence in the cytoplasm and nucleus of cells treated with FACSNPs. The greater intracellular distribution of FACS NPs through Folate receptor-mediated endocytosis is most likely the reason for their stronger cellular binding and subsequent absorption. The observed results suggest that the folate receptors mediated the enhanced cellular absorption of FACS NPs. The final step involves treating the wound healing assay (WHA) with 20 µg/ml FACS NPs within 24 hours, delaying or reducing migration. This suggests that chitosan-based FACS NPs encourage wound healing and inhibit cell migration(18) An established in vitro technique for evaluating cellular migration and proliferation—processes crucial to tissue regeneration and cancer metastasis—is the wound healing assay (33).

Nanosystem is a system where a plant extract is loaded onto nanoparticles, creating a delivery system with enhanced therapeutic properties (34) The study conducted by Gavamukulya et al. (14) integrated *A. muricata* with nanotechnology, as nanosystems enable the delivery of bioactive compounds at optimal concentrations throughout the treatment period, facilitating targeted action at specific sites and enhancing the compounds' therapeutic efficacy. To investigate the anticancer properties of green-generated AgNPs (silver nanoparticles) derived from ethanolic extracts of *A. muricata* fruits (AgNPs-F) and leaves (AgNPs-L) on various cancer cell lines, we concentrated on examining the impact on cervical cancer cell lines. According to the findings, AgNPs-F outperformed the conventional medication 5FU (5-fluorouracil) regarding selectivity index. This suggests that using AgNPs-F is safer than using 5FU. Drug selectivity has been described as one of the most essential characteristics of any effective treatment plan. AgNPs-L's selectivity index was significantly lower than the conventional medication 5FU. Therefore, it is clear from the current results, while being in the same selectivity index range, AgNPs-L are far more hazardous than the 5FU (14).

AgNPS-L exhibits a higher CASP9 expression level than untreated cells, but lower than 5FU as a positive control (14). CASP9 encodes the upstream caspase gene for the intrinsic route of apoptosis, which is called CASP9 (35,36). This gene must be upregulated in cancer cells in order to reduce the number of cancer cells. CXCL1 and CXCR2 expression should be reduced in contrast to CASP9. When compared to other genes, the expression of AgNPS-L is the lowest during treatment (14). The chemokine CXCL1 activates a signaling pathway called the CXCL1-CXCR2 axis by binding to its primary receptor, CXCR2. By encouraging tumor cell migration and invasion, promoting angiogenesis, and producing an immunosuppressive tumor milieu, this axis accelerates the growth of tumors (37,38).

Another nanotechnology was employed by Astirin et al. (17) using *Caesalpinia sappan* L. and *A. muricata* leaves extract. The experiment showed notable cytotoxic effects by inducing necrosis and apoptosis, as determined by flow cytometry. Interestingly, Nano-SL (Nano-Soursop Leaves) maintained a more noticeable apoptotic impact while exhibiting reduced general cytotoxicity compared to the control and *C. sappan* extract. According to these results, the nano formulation improves the bioactive chemicals from *A. muricata*'s selective delivery, which may increase its anticancer effectiveness while lowering its toxicity to healthy cells (15). The observed necrotic and apoptotic effects of Nano-SL are consistent

with other studies outlining *A. muricata's* mechanism of action. Potent inhibitors of mitochondrial complex I, Annonaceous acetogenins found in leaves, interfere with ATP synthesis and trigger intrinsic apoptotic pathways (30).

Besides acetogenins, there are numerous bioactive compounds in *A. muricata*. Stigmasterol (STML), one of the bioactive compounds of *A. muricata*, has cytotoxic, anticancer, anti-inflammatory, and antioxidant properties (39). Ahamed et al. (16) examined the anti-HeLa effects of STML extracted from *A. muricata* leaves. According to this study, STML from *A. muricata* leaves, showed powerful anticancer activities (16). In HT-22 cell culture, STML has been linked to the ability to provide neuroprotection by inhibiting signaling pathways implicated in glutamate-induced damage (39). AmeliMojarad et al.'s study showed that stigmasterol might cause breast tumor cells to undergo apoptosis by suppressing gene expressions of Bcl-XL and Bcl-2 (40).

A. muricata's cytotoxic effects on cervical cancer HeLa cells were investigated in another study by Astirin et al (17). The outcome demonstrated that HeLa cell proliferation is inhibited by *A. muricata* fraction, isolation, and nanoparticles. The IC_{50} value of three different kinds of compounds is also calculated in this investigation. All studied substances were classified as antiproliferative because their IC_{50} values were less than 100 µg/mL. The IC_{50} value of the fraction and isolates was higher than that of the nanoparticles. Using flow cytometry to observe the spread of cell death by necrosis and apoptosis, the cytotoxic effect of the materials was further confirmed. The isolated form of both materials has a higher capacity to induce HeLa cell apoptosis than nanoparticles, which is consistent with the MTT assay findings. When HeLa cells were treated with soursop leaf isolates, the percentage of cell death due to necrosis and apoptosis increased. This demonstrates that active substances in soursop leaves, such as annonaceous acetogenins, cause cancer cells to necrotize by preventing them from metabolizing (17).

According to the results of this systematic review, *Annona muricata* leaves extract shows promising therapeutic potential in targeting cervical cancer through a variety of mechanisms, such as suppression of crucial oncogenic signaling pathways, induction of apoptosis, inhibition of cell proliferation, and modulation of oxidative stress (13,14,17,18,41). Bioactive chemicals, including acetogenins, alkaloids, and flavonoids mediate these anticancer effects (13,16,42). A. *muricata* leaf extract has been shown in numerous in vitro investigations to have intense cytotoxic and pro-apoptotic action against cervical cancer cell lines like HeLa, but to have little cytotoxicity against normal cells (43). Nevertheless, despite these promising preclinical results, there are currently insufficient clinical investigations assessing the pharmacokinetics, safety, and effectiveness of *Annona muricata* leaf extract in people. Therefore, before it is included in clinical cancer practice, additional carefully planned clinical trials are necessary to verify its safety profile, ideal dosage, and possible synergistic interactions with conventional chemotherapeutic medicines.

4. Conclusion

The findings of this review indicate that the bioactive constituents of *Annona muricata* exhibit significant anticancer potential. Extracts of *A. muricata* demonstrate cytotoxic activity, induce apoptosis, upregulate p53 gene expression, and downregulate anti-apoptotic genes. Among its key bioactive compounds, A. *muricata*'s acetogenins exert their effect by inhibiting mitochondrial complex I, thereby reducing ATP synthesis, disrupting oxidative phosphorylation, and triggering apoptosis. Additionally, stigmasterol contributes to the plant's cytotoxic, anticancer, anti-inflammatory, and antioxidant properties.

Compliance with ethical standards

Acknowledgments

The authors would like to thank the Faculty of Medicine, Universitas Jember, and all the parties who supported and offered deep insight into this literature.

Disclosure of Conflict of interest

The authors declare no conflicts of interest.

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