Pomegranate: the Savier of Ovarian Cancer

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***Abstract*—Ovarian cancer is the fifth most common cause of death for women overall and the leading cause of death for women diagnosed with gynecological cancers. The majority of cases are diagnosed at an advanced stage, which results in poor outcomes for this disease. The key early detection strategies include transvaginal ultrasound, a laboratory marker such as the cancer antigen-125 assay, and a detailed gynecological evaluation; however, anti-angio genic bevacizumab and Poly (ADP-ribose) polymerase (PARP) inhibitors have gained traction in the management of this gynecological malignancy in the last ten years. After the initial treatment, a high rate of recurrence has been noted. The majority of these relapsed cases are known to have a higher rate of treatment failures and are less treatable. Therefore, there is an urgent need for innovative treatment methods based on a deeper understanding of the molecular characteristics of this malignancy as well as efficient preventive and detection strategies. In addition to reviewing the epidemiology and risk factors of ovarian cancer, this article discusses some recent ongoing studies and emphasizes the evaluation and multidisciplinary approach in the care of this condition. We use here pomegranate**

***Index Terms*—Ovarian cancer, Pomegranate, Menopause,Tumor**

Objective

I. To aid in early diagnosis and treatment, distinguish the symptoms of ovarian cancer from those of other gynecological disorders(1).
II. To Use the proper techniques, such as transvaginal ultrasonography, pelvic exams, and tumor marker tests, to screen patients for ovarian cancer.(2)
III. To Use multimodal therapy, imaging scans, and biopsy as part of evidence-based ovarian cancer diagnosis and treatment methods (3).
IV. To Utilize inter professional team techniques to enhance ovarian cancer patients' care coordination and results (4).

I. INTRODUCTION

Both epithelial and non-epithelial ovarian cancers are classified as ovarian cancers (5). Over 95% of ovarian cancers are epithelial, whereas non epithelial ovarian cancers (such as germ cell, sex-cord stromal, and small cell ovarian cancers) make up about 5% of all ovarian cancers (6). High-grade serous, low-grade serous, clear cell, endometrioid, and mucinous ovarian cancers are among the subtypes of epithelial ovarian cancers that are separated by histologic classification because the subtypes can affect patient outcomes, therapy, and diagnostic evaluation(7).

Ovarian cancer is the primary cause of mortality among women diagnosed with gynecological cancers and the second most frequent gynecologic malignancy in the United States, according to the Centers for Disease Control and Prevention. Ovarian cancer is the third most prevalent gynecologic cancer in the world (8).

In the United States, ovarian cancer ranks fifth among all cancers that kill women, and it ranks eighth globally (9). The vague clinical symptoms of ovarian cancer and the absence of preventative screening techniques undoubtedly contribute to the illness's high death rate by delaying diagnosis; the majority of patients are diagnosed with advanced-

stage disease (10). Advanced age is the biggest risk factor for ovarian cancer, which primarily affects postmenopausal women (11).

Clinical assessment, imaging examinations, and tumor markers are the main tools used to evaluate any ovarian mass in order to identify the mass's characteristics and determine the patient's risk factors for malignancy; an ovarian cancer diagnosis is confirmed by histology. Treatment strategies are determined on the stage and histology of the tumor as well as patient characteristics (such as comorbidities and prior treatments) (12). At the moment, systemic chemotherapy and surgical debulking are usually advised, either in conjunction with or apart from targeted therapies (13). Antiangiogenic bevacizumab, polyadenosine diphosphate (ADP)-ribose polymerase (PARP) inhibitors, and immunotherapy are examples of targeted therapy (14). Furthermore, new approaches to the treatment of ovarian cancer include hot intra peritoneal chemotherapy, interval surgical debulking, and neo adjuvant therapy (15). A high recurrence rate and mortality rate, however, persist despite advancements in ovarian cancer treatment, highlighting the need for inter professional management, effective prevention and detection strategies, and novel treatment modalities founded on a deeper comprehension of the molecular features of ovarian cancer.

Risk Factors for Ovarian Cancer

Although the exact cause of ovarian cancer is unknown, a number of factors have been found to raise the risk of developing the disease (16). The following are risk factors for ovarian cancer:

i. Older age
ii. Menarche at an early age
iii. Menopause's late start
iv. Family background
v. The absence of nulliparity
vi. Being overweight
vii. Use of perineal talcSmoking
viii. Endometriosis
ix. Hormone replacement treatment

Fig No.1 Risk Factor of Ovarian cancer

A higher risk of ovarian cancer is linked to factors that enhance ovulation throughout one's lifespan, such as nulliparity, early menarche, or late menopause (17). The precise etiologic process is unknown, though. Furthermore, it is believed that oxidative stress and deoxyribonucleic acid damage caused by inflammatory diseases (such as endometriosis and obesity) contribute to the development of ovarian cancer (18). A substantial risk factor for ovarian cancer is a positive personal or family history of breast or ovarian cancer. One common underlying reason of a person's predisposition to cancer is germline mutations in the BRCA1 or BRCA2 genes (19). Mismatch repair genes in Lynch syndrome, tumor protein p53 (TP53) in Li-Fraumeni syndrome, STK11 in Peutz-Jeghers syndrome, CHEK2, RAD51, BRIP1, and PALB2 are among the other hereditary cancer syndromes linked to gene mutations that also raise the risk of ovarian cancer(20). Based on detected alterations in the distal epithelium in fallopian serous tubal intraepithelial carcinoma, an HGSC precursor, recent results indicate that high-grade serous ovarian cancer (HGSC) may have its genesis in the fallopian tube(21). Although studies have not shown that suggested ovarian cancer screening procedures are helpful, several organizations have agreed that it is appropriate to offer these high-risk people a variety of screening options.

Epidemology

According to study findings, a woman has a 1.1% chance of getting ovarian cancer during her lifetime up to age 95(22). Over 19,000 new cases of ovarian

cancer were detected in the United States in 2022, and over 12,000 people were thought to have died from the disease (23). Additionally, there are age-related differences in the incidence of ovarian cancer subtypes (24). Women aged 45 to 50 years had the highest incidence of low-grade endometroid ovarian cancer, while those aged 60 to 65 years have the highest incidence of high-grade serous ovarian cancer (25). Women between the ages of 55 and 60 are most likely to develop clear-cell ovarian cancer (26). Non-Hispanic White women have the highest incidence of low-grade endometrioid and high-grade serous malignancies; Clear cell cancer is more common in Asian/Pacific Islander women, while non-Hispanic Black women have the lowest incidence of all ovarian cancer subtypes. The 5-year survival rate for early-stage ovarian cancer is 93.1%, while the 5-year survival rate for advanced-stage disease is 30.8%. The recurrence risk for stage I ovarian cancer is less than 10%, while 90% of women with stage IV ovarian cancer experience recurrence (27)

II. SYMPTOMS

- Bloating or a swollen feeling in the stomach
- Feeling full quickly after eating
- Frequent or urgent Pelvic pain
- abdominal pain or cramping
- Unexplained weight loss
- Fatigue (28)

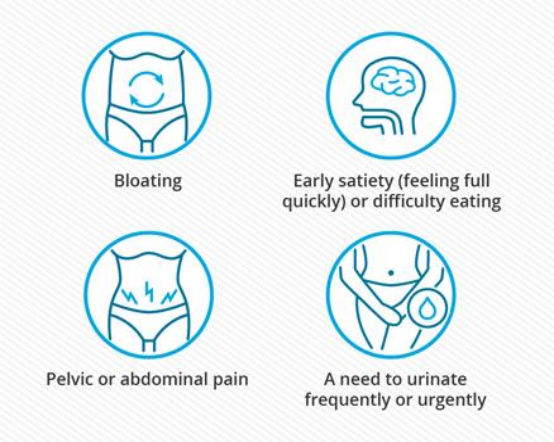


Fig No 2.symptoms of ovarian cancer

Fruits with Potential Anti-Cancer Activity

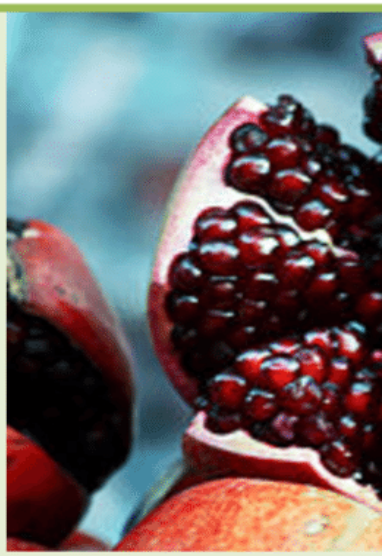
1.Pomegranate

Image No.1 pomegranate

The biological source of pomegranate is the plant Punica granatum L., which belongs to the family Lythraceae(29)

Pomegranate

Kingdom	Plantae
Division:	Magnoliophyta
Class:	Magnoliopsida
Subclass:	Rosidae
Order:	Myrtales
Family:	Lythraceae
Genus:	*Punica*
Species:	***P. granatum***



fruit

Image No.2 Botanical profile of Pomegranate

Chemical Constituents with Anti-Ovarian Cancer Potential

- Polyphenols
  - *Punicalagin* and *punicalin*: Hydrolyzable tannins with strong antioxidant and anti-inflammatory effects(30)
  - *Ellagic acid* and *gallic acid*: Known to induce apoptosis and inhibit cancer cell proliferation(31)
  - *Flavonoids*: Includes quercetin, kaempferol, catechin, epicatechin, and rutin—modulate cell signaling and oxidative stress (32).
- Phenolic **Acids**
  - *Caffeic acid*, *ferulic acid*, *p-coumaric acid*: Contribute to antioxidant and anti-proliferative activities(33)
- Anthocyanins
  - Provide antioxidant effects and may influence cancer cell cycle regulation(34)
- Sterols **and Alkaloids**
  - Present in smaller amounts but may support anti-cancer mechanisms(35)
- Punicic **Acid**
  - Found in pomegranate seed oil; a conjugated fatty acid with anti-inflammatory and anti-tumor properties(36)

Compound Compound	s	Class	Specific Molecules	Role in Ovarian Cancer Treatment	Role in Ovarian Cancer Treatment Class
Phenolic Acids			Ellagic acid, gallic acid, caffeic acid, ferulic acid, p-coumaric acid		Antioxidant, anti-inflammatory, DNA damage protection
Hydrolyzable Tannins			Punicalagin, punicalin, ellagitannins		Induce apoptosis, inhibit proliferation, modulate cell cycle

Flavonoids	Catechin, epicatechin, quercetin, rutin, kaempferol Delphinidin, cyanidin, pelargonidin derivatives Estrone, estradiol, testosterone	Suppress tumor growth, regulate signaling pathways Antioxidant, modulate oxidative stress Influence hormone-related cancer pathways
Anthocyanins	Delphinidin, Cyanidin, pelargonidin derivatives	Antioxidant, Modulate oxidative stress
Steroids & Phytoestrogens	Estrone, estradiol, testosterone	Influence hormone-related cancer pathways

Chart NO.1Chemical Constituents with Anti-Ovarian Cancer Potential

Mechanisms of Action Against Ovarian Cancer

Cell Cycle Arrest: PPE increases levels of CDKN1A (p21), halting cancer cell proliferation

Apoptosis Induction: Promotes programmed cell death in ovarian cancer cells (e.g., OVCAR-3 line)
Oxidative Stress Modulation: Acts as antioxidant in healthy cells and prooxidant in cancer cells, disrupting their survival

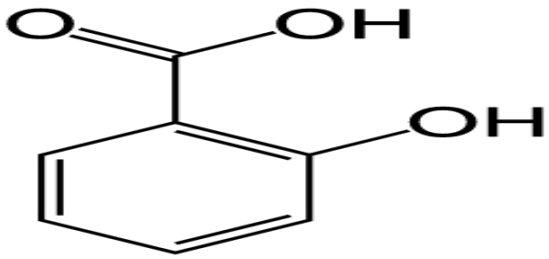
Growth Factor Suppression: Reduces TGF-β2 and EGF levels and their receptors (TGFBR2, EGFR) in cancer cells
Steroidogenesis Influence: Stimulates estradiol secretion in non-cancerous ovarian cells, potentially supporting hormonal balance (37)

1 phenolic acid
It acts against ovarian cancer, with a focus on their molecular targets, mechanisms, and therapeutic relevance. (38)

What Are Phenolic Acids?
Phenolic acids are a subclass of plant-derived polyphenols, mainly divided into:
Hydroxybenzoic acids: e.g., *gallic acid*, *protocatechuic acid*, *salicylic acid*

Hydroxycinnamic acids: e.g., *caffeic acid*, *ferulic acid*, *p-coumaric acid (39)*

They're found in fruits like pomegranate, berries, and vegetables, and are known for their antioxidant, anti-inflammatory, and anticancer properties. (40)

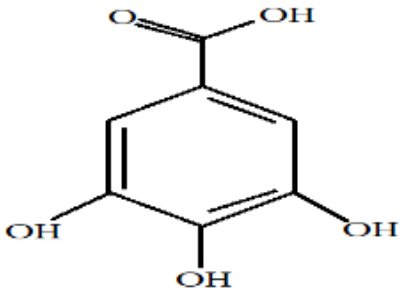


Strcture no 1. Phenolic acid

2.Hydrolyzable tannins—especially gallotannins and ellagitannins—are a class of polyphenolic compounds found in plants like pomegranate, Terminalia chebula, and Phyllanthus niruri(41). They've gained attention for their potent anti-ovarian cancer effects through multiple molecular mechanisms. (42)

🌿 What Are Hydrolyzable Tannins?

These are tannins that can be hydrolyzed into sugars and phenolic acids (like gallic acid and ellagic acid) (43). Two major types:
Gallotannins: Esters of gallic acid with glucose (e.g., tannic acid, corilagin, chebulagic acid)
Ellagitannins: Esters of hexahydroxydiphenic acid with glucose (e.g., punicalagin, pedunculagin)(44)



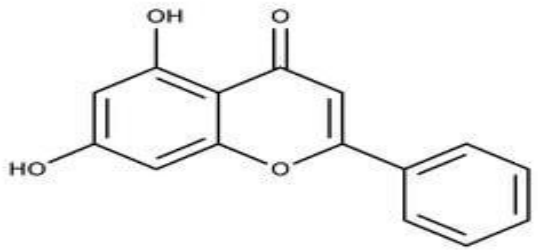
Strcture no 2. Hydrolyzable tannins

3.Flavonoids

Flavonoids are a diverse group of plant-derived polyphenolic compounds that have shown significant anti-ovarian cancer potential through multiple biochemical and cellular mechanisms (45). Let's unpack their types, molecular actions, and therapeutic relevance in detail (46).

What Are Flavonoids?

Flavonoids are secondary metabolites found in fruits, vegetables, tea, wine, and medicinal herbs. (47)



Stru.no.3. Flavonoids

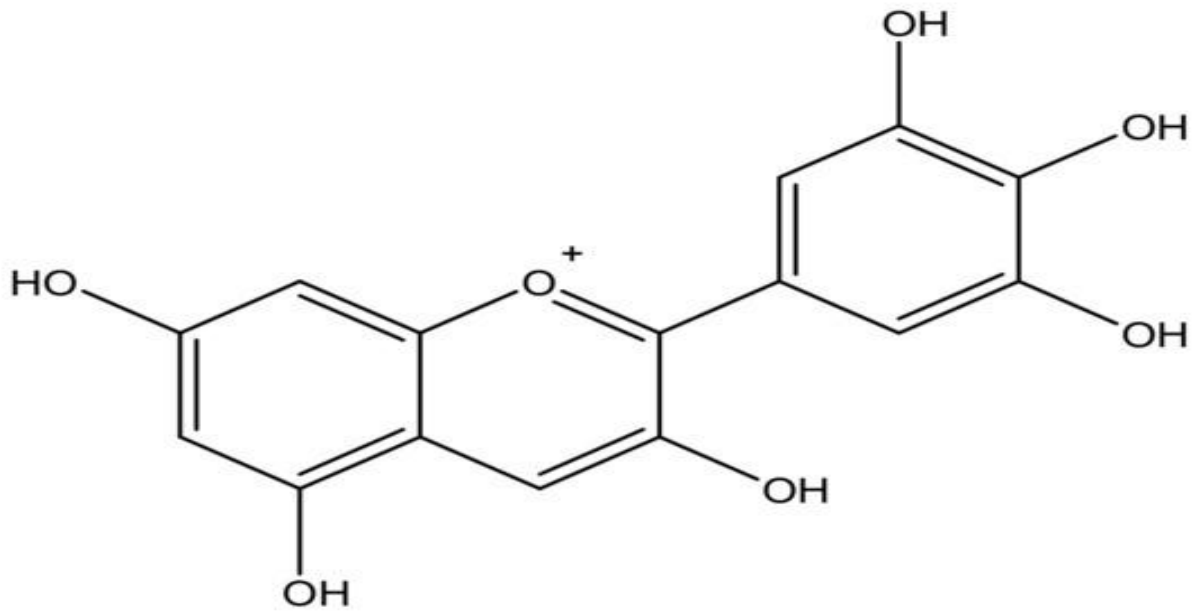
4.Anthocyanins

Anthocyanins are vibrant plant pigments responsible for the red, purple, and blue hues in many fruits and vegetables—and they're emerging as powerful allies in the fight against ovarian cancer (48)

What Are Anthocyanins?

Anthocyanins are a subclass of flavonoids found in the cell vacuoles of plants. They exist as glycosides of anthocyanidins (49)

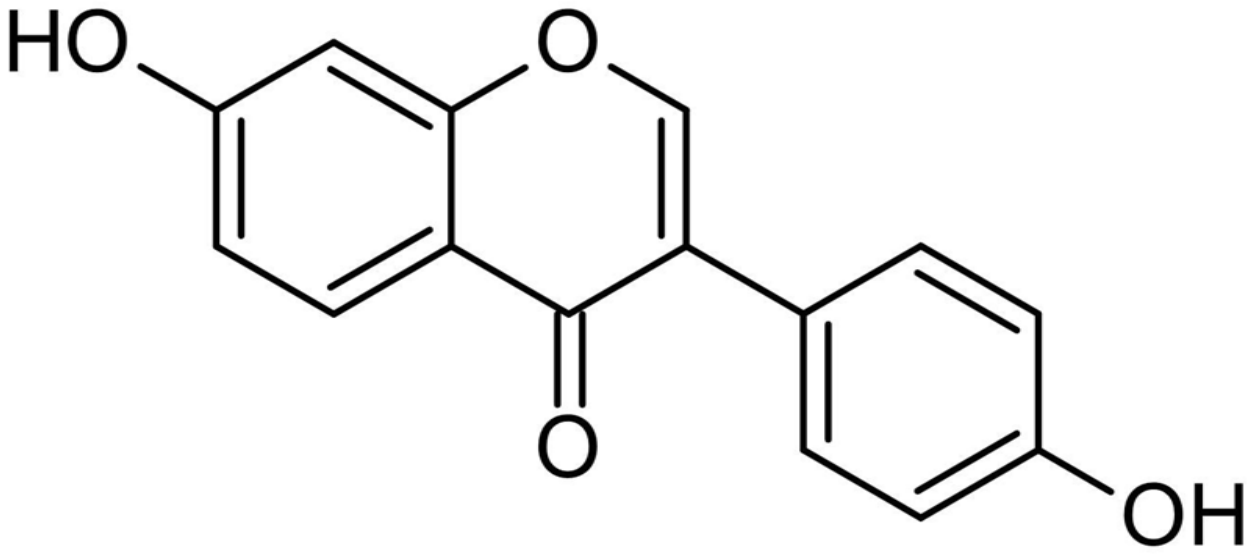
Their antioxidant capacity is influenced by the number and position of hydroxyl and methoxy groups on their B-ring. (50)



Stru.no 4. Anthocyanins

5.Steroids & Phytoestrogens

Steroids, particularly glucocorticoids and sex steroids, are used in ovarian cancer treatment for both therapeutic **and** supportive (51)



Stru.no 5. Steroids & Phytoestrogens

III. CONCLUSION

Ovarian cancer remains one of the deadliest gynecological malignancies due to late-stage diagnosis and high recurrence rates. Early detection through imaging and tumor markers is critical, but treatment remains challenging, especially in recurrent cases. Advances in targeted therapies—such as PARP inhibitors and bevacizumab—have shown promise. Understanding molecular pathology, implementing multimodal diagnostic strategies, and enhancing interprofessional care coordination are vital for improving outcomes. Additionally, emerging natural compounds like those found in pomegranate offer potential in adjunctive therapeutic strategies.

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