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Review Article:

Durian: The King of Fruits with Potential Anti-Cancer Properties – A Scoping Review of Current Findings

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Abstract

Context: The king of fruits of Southeast Asia, durian, which is rich in bioactive chemicals, has drawn interest due to its possible anticancer effects.

Evidence Acquisition: This review paper investigates the latest scientific findings regarding the fruit's potential as an anticancer agent. There are research gaps, especially in the absence of in vivo studies to corroborate the cytotoxic effects of durian extract on different cancer cell lines.

Results: In vitro studies have shown these effects on cancer cell lines. The study indicates future directions, including in vivo models, mechanistic investigations, and investigation of combination therapy. It emphasizes the need for more research to clarify the molecular processes behind durian's anticancer properties.

Conclusion: By filling these knowledge gaps, durian has the potential to become a valuable natural cancer-fighting agent.

Keywords: Anti-cancer, Durian, Durio, Flavonoids, King of fruits

1. Context

The seasonal tropical fruit known as durian, or *Durio zibethinus L.* in scientific terms, is a climacteric fruit native to Southeast Asia, specifically in Malaysia, Thailand, Philippines, and Indonesia. The mature durian fruit is referred to as the "king of fruits" in the area because of its distinct flavour and scent [1]. *Durio testudinarius Becc., Durio graveolens Becc., Durio grandiflorus Kosterm. & Soegeng, Durio dulcis Becc., Durio oxleyanus Griff., Durio kutejensis Hassk. & Becc.,* and *Durio lowianus Scort.* ex-King are the seven species noted for producing edible fruit, aside from Durio zibethinus (Figure 1) [2]. However, in this review, we will only discuss Durio zibethinus L. since it is widely researched. In addition to being high in carbohydrates, durian fruit pulp also includes proteins, fats, fibers, B vitamins, vitamin C, and minerals including calcium, zinc, and salt [3]. Moreover, myristic acid, linoleic acid, stearic acid, and palmitic acid may be found in the pulp [1]. Anti-obesity [4], anti-cancer, anti-cardiovascular [5], and antioxidant [6] actions are among the medical benefits of durian fruits. Anxiety, tension, and sadness have all been claimed to be lessened by durian pulp [7]. Extracts from durian fruit have been shown to suppress the proliferation of breast cancer cell lines [8] and to slow the growth of Calu-6 and SNU-601 cell lines [9].

Since fruits are a natural source of bioactive substances such as flavonoids, carotenoids, acetogenins, polyphenols, and stilbenes that have

been demonstrated to be effective against cancer cells both in vitro and in vivo, it is crucial to investigate these sources for cancer treatment. These substances may be helpful in the prevention of cancer because they can change cellular responses, impact epigenetic alterations, and regulate protein expression. Furthermore, compared to manufactured substances, natural compounds derived from fruits and vegetables are typically linked to fewer adverse effects [10].

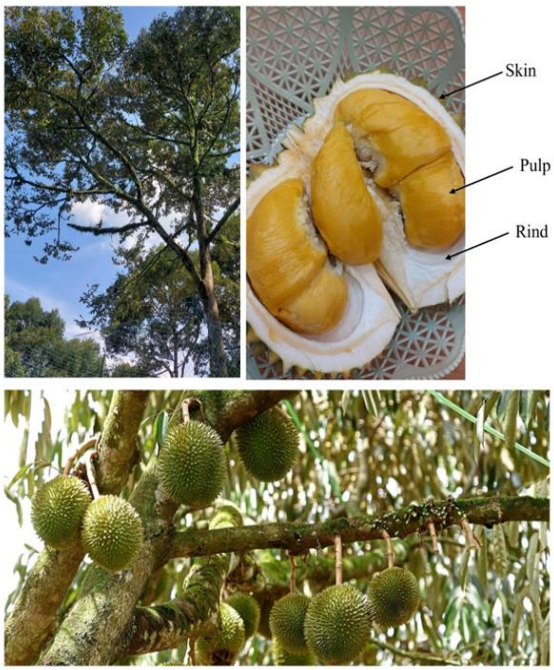

Figure 1. Shows the image of durian tree and durian fruit

This article reviews original research and analyses studies on the anti-cancer properties of durian. Research on bioactive compounds such as flavonoids, polyphenols, carotenoids and others has been rigorously examined through a literature review to better understand the mechanisms behind durian's potential anti-cancer effects. Data collection and literature review were conducted using Google Scholar and PubMed.

2. Evidence Acquisition

Nutritional Profile and Bioactive Compounds in Durian

The tropical fruit durian is renowned for both its distinct flavour and nutrient makeup. It has a creamy texture, a sweet-bitter flavour, and a high energy density [11]. Ascorbic acid, carotenoids, and flavonoids are also abundant in durian, adding to its nutritional worth. However, depending on the type and the growing location, durians can have different nutritional profiles [12]. Bioactive substances found in durian include flavonoids, carotenoids, and polyphenols. It has been demonstrated that these substances have probiotic, antioxidant, and antiproliferative properties. In experimental animal models, durian extract has been shown to lower cholesterol and blood glucose levels, indicating possible health advantages [11].

Flavonoids

One type of bioactive substance included in durian is flavonoids. Their antidiabetic and antioxidant qualities have been demonstrated [13]. High flavonoid concentration has been found in extracts from durian fruit rinds; the greatest flavonoid content of 82.17 mg QE/g extract was obtained by extracting the fruit at 60°C with 75% ethanol and macerating it for 24 hours (Table 1)[13].

Table 1. Flavonoid concentration for each part of Durian

Part of Durian	Flavonoid Concentration	References
Seeds	nd	-
Skin	(12.91 ± 0.03) mg CAE/g.DW	[17]
Rind	82.17 mg QE/g	[18]
Pulp	271.11 mg QE/g	[18]

Polyphenols

Another group of bioactive substances present in durian is polyphenols. They can enhance the fruit's overall nutritional profile and have shown to possess antioxidant qualities [12].

Carotenoids

Fruits and vegetables obtain their vibrant colors from compounds called carotenoids. Carotenoids are found in durian, which enhance its nutritional value and may offer health advantages [11].

Extracts from Durian Seeds

Essential bioactive components including carotenoids, polyphenols, flavonoids, and phenolic

acid are present in durian seed extracts and have been shown to have significant antioxidant activity. These extracts offer potential advantages for the environment and can be utilised as sources of functional food [14].

Extracts from Durian Skin

The beneficial components of durian skin extracts, such as flavonoids, which function as antioxidants and antibacterials and help brighten and renew skin, are utilised to manufacture cosmetic preparations like liquid soap [15].

Rinds of Durian Fruit

Flavonoid extraction from durian fruit rinds has been optimised; the greatest flavonoid concentration of 82.17 mg QE/g extract was obtained at 60°C with 75% ethanol and a 24-hour maceration period [13]. Following liquid-liquid extraction, the crude ethanolic extract was separated into three fractions; the CHF fraction had the greatest concentration of flavonoids (271.11 mg QE/g extract) and quercetin (1,006.19 µg/g extract) [13].

Pulp from Durian Fruit

Nutrient-rich durian fruit pulp has a lot of protein, fat, carbs, and dietary fibre. Depending on the durian type, the protein content varies; some have larger quantities than others. In comparison to its animal-based equivalents, durian fruit pulp likewise has lower calorie values and higher levels of carbohydrates and dietary fibre [16].

Antioxidant Activity and Relevance to Anticancer Properties

Antioxidant studies revealed that durian fruit extracts had strong antioxidant activity against nitric oxide and ABTS, but tests such as FRAP, DPPH, and others demonstrated reduced antioxidant capacity in comparison to standard [19]. Because antioxidants scavenge reactive oxygen species (ROS) and other free radicals that can harm cellular proteins, lipids, and DNA, antioxidants are essential in halting the development of cancer [20]. In actively developing cancer cells, natural antioxidants like those in durian can eliminate excess free radical intermediates and postpone oxidative reactions. Antioxidants can prevent cancer, but their effects are complicated and vary depending on the kind of antioxidant, the type of cancer, and when antioxidants are administered [20]. In comparison to snake fruit (110.4+/-7.9 and 1507.5+/-70.1 µM TE/100 g of FW) and mangosteen (79.1+/-5.9 and 1268.6+/-62.3 µM TE/100 g of FW), durian was shown to have stronger antioxidant activity (228.2+/-13.4 and 2016.3+/-81.1 µM TE/100 g of FW) [21].

According to one study that looked at the antioxidant capacity of durian shell extract, the extract showed significant antioxidant properties that were dose-dependent [22]. An additional investigation refined the flavonoid extraction parameters from durian fruit rinds and assessed the biological properties of the extracts high in flavonoids, demonstrating noteworthy antioxidant activity [13]. There are other health advantages of durian besides its antioxidant qualities. It has been demonstrated to have antidiabetic potential by inhibiting the enzymes α-amylase and α-glucosidase [22]. Additionally, the anti-inflammatory and anti-cancer effects of durian have been discovered [13]. When durian's antioxidant activity was compared to that of other fruits, such as mangosteen and snake fruit, it was shown to be considerably greater [21]. This implies that eating durian might be a good way to get antioxidants in your diet.

Anticancer properties of Durian

Antioxidants are essential for avoiding free radical-induced cellular damage, which is one of the factors that leads to the development of cancer. Durian fruit extract showed anticancer properties against Chang liver cell lines in the same investigation, indicating its potential as a source of anticancer agents [19]. The identification of new compounds in durian shells provides more evidence for the fruit's potential as an anticancer agent. From durian shells, scientists have discovered novel triterpenoids, phenolics, and glycoside esters, several of which had strong anti-inflammatory properties1. Since inflammation is a recognised factor in the development of cancer, substances that block inflammatory pathways may help prevent or treat the disease. Furthermore, a great deal of research has been done on the antioxidant and anti-inflammatory properties of different durian fruit components [23]. After analysis, flour extracts from these sections were shown to have anti-inflammatory and antioxidant qualities, as shown by their capacity to prevent stimulated cells from producing nitric oxide (NO) [24]. The suppression of NO synthesis is important as elevated NO levels have been linked to several cancers.

A separate study examined the antioxidant characteristics of durian fruit at various ripening stages. Ripe durian was shown to have much greater concentrations of chemicals linked to antioxidant activity, such as polyphenols, flavonoids, anthocyanins, and flavonols [25]. This implies that by increasing the number of advantageous phytochemicals in durian, the ripening process may improve the fruit's ability to fight cancer. Another tropical fruit, rambutan, was also contrasted with durian in terms of its anti-inflammatory and

antioxidant properties. Tumour necrosis factor-alpha (TNF-α) and interleukin-8 (IL-8) were two pro-inflammatory cytokines whose release was suppressed more effectively by durian extracts than by reactive oxygen species (ROS) [24]. These results suggest that there may be a greater chance of developing functional foods with anticancer properties from durian.

In a study by Abdul et al. in 2023, PI staining and Annexin V-FITC staining demonstrated that D. zibethinus pulp extracts induced apoptosis in the current investigation. The extracts' flavonoid content may be the cause of this apoptotic induction [26,27]. Both in vivo and in vitro studies of flavonoids reveal anticancer characteristics, including antileukemic effects [28]. Stimulation of apoptosis and disturbance of the cell cycle result in inhibition of the growth of cancer cells [29]. Several oncogenes and oncoproteins work in concert and against one another to cause the coordinated process known as apoptosis. One method for treating cancer is to induce the apoptotic process. According to this study, the intrinsic route appeared to be how the methanolic extract of D. zibethinus fruit pulp induced apoptosis. The activation of caspase-9, which in turn activates caspase 3, is a step in the intrinsic apoptotic cascade. Thus, to verify that caspases 9 and 3 were activated, Western blotting was done. The pro-apoptotic Bax protein and caspases 9 and 3 were significantly elevated by the methanolic extract of D. zibethinus fruit pulp. This demonstrated that D. zibethinus fruit pulp methanolic extract induced an inherent apoptotic pathway in HL-60 cells [30].

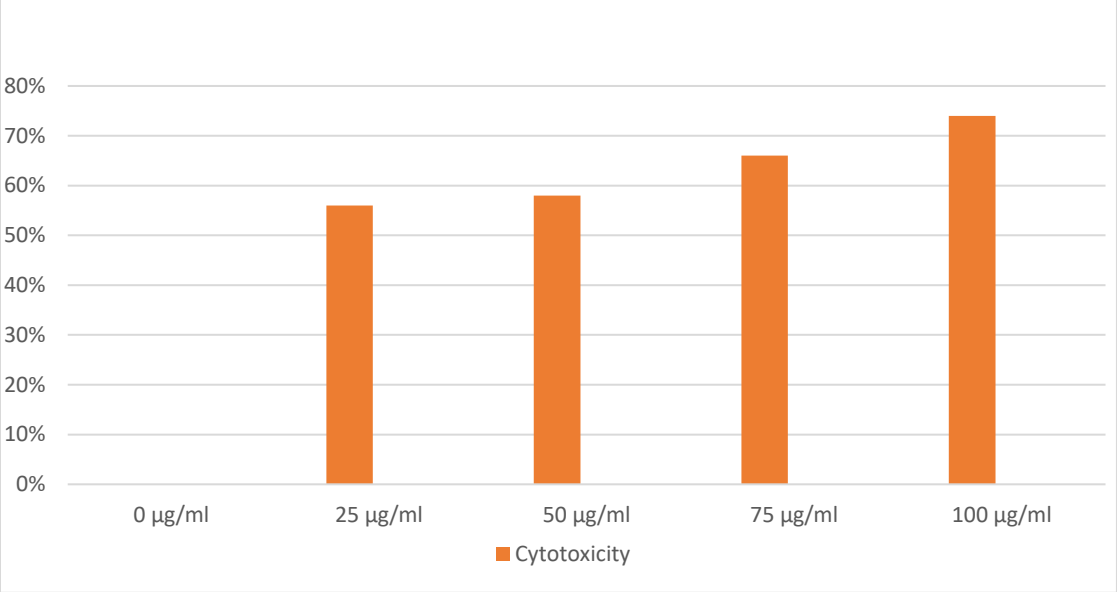

Figure 2. Cytotoxicity of Durian Fruit Extracts

In another study, the cytotoxicity of durian fruit extract was assessed in vitro against Chang liver cells at various doses (0, 25, 50, 75, and 100 µg/ml). The extract from durian fruit exhibited dose-dependent cytotoxicity. At 100 µg/ml, the greatest cytotoxicity (74%) was observed, while at 75 µg/ml and 50 µg/ml, respectively, the moderate cytotoxicity (66%, 58%) was detected. The durian fruit extract's lowest cytotoxicity (56%) was measured at 25 µg/ml. Contrary to expectations, the control showed no cytotoxic action (Figure 2) [19]. Four new phenolics with strong NO inhibitory and antioxidant properties were found through additional investigation into the bioactive components of durian peel [31]. These phenolics demonstrated the promise of durian-derived chemicals as natural alternatives for cancer prevention since they were more effective than the widely used anti-inflammatory medicine indomethacin in reducing NO generation.

Bioactive substances such as glycoside esters, triterpenoids, phenolics, and flavonoids support its anti-inflammatory and antioxidant properties, which are critical in the fight against cancer. Although the studies mentioned offer insightful information, more investigation is required, including clinical trials, to completely comprehend the pathways via which durian chemicals exercise their anticancer effects

and to assess their effectiveness in people. However, the available data suggests that durian is a fruit with both nutritional value and possible medicinal uses in the battle against cancer [23–25,31,32].

3. Result

Future Directions

Notwithstanding the encouraging results, there are several limitations in the present study about the anticancer potential of Durian that require attention. Most investigations on the anticancer effects of durian have been carried out in vitro. In vivo research is desperately needed to validate these biological processes in a live thing [23,32]. Liver cancer cell lines have been the main focus of current research. Research on a range of cancer types should be included to completely comprehend durian's anticancer potential [32]. Although durian's anti-inflammatory and antioxidant qualities have been established, little is known about the underlying processes that underlie its anticancer effects [23,32]. The processing of durian extracts is not standardised, which may cause variations in the outcomes. For research to be comparable and reproducible, standardised procedures are required. Little is known about the bioavailability or metabolism of the bioactive chemicals found in durian in the human body. Comprehending these facets is vital in assessing the fruit's medicinal possibilities. There has been little research done on the usage of durian shells, thus further research is needed to determine the ecological effects of using this byproduct for medical purposes [23,32].

To confirm the anticancer effects seen in vitro, animal models should be used in future studies. This will aid in comprehending the bioactive chemicals included in durian's pharmacokinetics and pharmacodynamics. To find out how effective durian is for all forms of cancer, researchers need to look into how it affects various cancer cell lines and tumours. To understand how the chemicals in durian exert their anticancer properties, comprehensive mechanistic investigations are necessary. This may entail researching how gene expression, apoptosis, and signalling pathways are altered. Creating standardised extraction procedures can guarantee uniformity in the profiles of bioactive compounds in durian extracts utilised in studies [23,32].

4. Conclusion

In conclusion, durian is a nutrient-dense fruit with a unique flavour profile and a range of bioactive compounds that offer potential health benefits. Its nutritional profile and bioactive compounds can vary depending on the variety and region of cultivation. Durian shell and fruit rinds have been used in green synthesis and for the extraction of bioactive compounds, while durian seed and skin extracts have been used in functional food and cosmetic preparations. The antioxidant activity of durian has been attributed to its high phenolic content, particularly flavonoids and phenolic acids. Research has indicated that durian possesses noteworthy anti-inflammatory and antioxidant qualities, making it a promising source of anticancer chemicals. However, the paucity of in vivo investigations and a thorough knowledge of the processes involved impedes the translation of in vitro results into therapeutic applications. To fully realise durian's therapeutic potential and make its advantages available for cancer prevention and therapy, future research are warranted to fill these gaps.

Ethical Considerations

Compliance with ethical guidelines

There were no ethical considerations to be considered in this research.

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Author's contributions

Conceptualization, Methodology, Software, Writing – Original Draft Preparation, Writing – Review & Editing, Visualization, Project Administration, and Funding Acquisition: Aayush; Data Curation, Validation, Formal Analysis and Investigation: All authors; Supervision and Resources: Abhikrishnan Gopakumar.

Conflict of interest

All authors have no conflicts of interest.

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