Penerbit Akademia Baru

Journal of Advanced Research Design

Journal homepage:
www.akademiabaru.com/ard.html
ISSN: 2289-7984

Bioresources of Anticancer and Potential Medicinal Compound from Coconut Waste

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ARTICLE INFO

Article history:
Received 14 June 2024
Received in revised form 9 August 2024
Accepted 22 August 2024
Available online 30 August 2024

Keywords:
Coconut wastes; anticancer; MCF-7; MTT assay

ABSTRACT

Cocos nucifera L. (family Arecaceae) commonly known as coconut is considered as an important fruit crop in tropical countries and are widely used for therapeutic and domestic purpose. They have effective properties such as antioxidant, antitumor, antiseptic and antimicrobial. The growing demand for green coconut water consumption and food industries cause the dumping of the shell and husk of this fruit, generating large amount of solid waste. This study utilized two parts of coconut waste which are shell and husk in order to determine the anticancer properties. Six different polarities of solvent were chosen. The anticancer activity *via* MTT assay showed that acetone extract of coconut shell exhibited the highest anticancer activity with 34.80 % of the cell was damaged at 10 mg/ml. Lowest cytotoxicity of 10.96 % was shown by chloroform extract of coconut shell at 3 mg/ml. Propanol extract of coconut husk exhibited the highest cytotoxicity (32.42 %) against MCF-7 and lowest cytotoxicity was demonstrated by methanol extract (12.11 %). GCMS analysis confirmed that the presence of major compounds such as dodecanoic acid (25.21 %), tetradecanoic acid (23.04 %), 1,4-bis(trimethylsilyl)benzene (19.42 %) and oleic acid (10.44 %) in the coconut shell; and dodecanoic acid (33.03 %), tetradecanoic acid (24.79 %), n-hexadeconoic acid (7.090 %) and (oxime-, methoxy-phenyl-(6.48 %) in the coconut husk. Therefore, coconut waste-by products excert potential medicinal properties suitable for further research in other health perspectives.

1. Introduction

Coconut, scientifically known as *Cocos nucifera*, is a significant fruit crop in tropical regions and is extensively farmed for both food industries and the consumption of green coconut water [1]. Its utilization is widespread across various parts of the globe, notably in coastal areas, owing to its medicinal and nutritional attributes. Nevertheless, despite its substantial economic importance, a large portion of the coconut's weight, around 80 to 85 %, including the shell and husk, is discarded within the coconut industry, resulting in a considerable waste output [2]. Coconut shells exhibit a

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https://doi.org/10.37934/ard.119.1.1626

composition akin to wood [3] and may require up to a decade to fully decompose [4]. The substantial volume of residues and the slow rate of decomposition of this waste can attract disease-carrying vectors like mosquitoes, flies, rats and cockroaches, thereby posing health risks to humans. Improper handling of such waste can lead to the spread of diseases such as dengue and cholera, as the accumulated waste may clog public drainage systems [5,6], contribute to air pollution and compromise the hygiene of public spaces [6].

The coconut fruit possesses distinctive characteristics, with its wall comprising three layers: the exocarp, mesocarp and endocarp [1,7,8]. The mesocarp is rigid and fibrous due to the extensive interconnection between phenolics, polysaccharides and lignin [7]. Research has indicated the utilization of various parts of the coconut as traditional remedies for different ailments in diverse regions globally. For example, coconut husks have traditionally served as herbal teeth-cleaning sticks, offering an eco-friendly alternative to plastic bristle brushes [9]. Moreover, coconut husks have been commonly employed in Brazil as a traditional treatment for diarrhoea and arthritis [10]. Furthermore, the coconut shell has been historically utilized as a source material for producing activated charcoal and liquid smoke [11].

Cancer is defined as the abnormal and unregulated proliferation and division of cells, triggered by various external factors like ionizing radiation or carcinogenic substances, as well as internal factors such as chronic inflammation and DNA mutations. The efficacy of anticancer properties derives mainly from their antioxidative and anti-inflammatory characteristics, facilitating the elimination of reactive oxygen species (ROS) and thereby preventing potential DNA harm or the liberation of pro-inflammatory agents [12].

Overcoming malignant cell eradication presents a substantial challenge in the oncology field. The tumor cells' ability to resist apoptosis and their robustness against therapeutic interventions persist as key factors contributing to the ineffectiveness of cancer therapy [13]. Despite the array of available antineoplastic medications, roughly 50 % of cancer patients encounter a temporary regression following treatment, yet eventually succumb to widespread metastasis [14].

According to Inyinbor *et al.,*[15] the presence of effective treatments for cancer is a subject of debate. Despite the existence of current remedies, the high cost of treatment is a growing concern for numerous cancer patients. Hence, the discovery of anticancer compounds in biomass waste is considered advantageous, particularly for individuals in developing nations where cancer treatment expenses are exorbitant.

Previous studies have explored the cytotoxic effects of coconut husk and shell [1,14]. However, these investigations were confined to individual components of the coconut (seeds, rind or the entire fruit). Additionally, the utilization of diverse solvent extractions against cancer cells was also restricted.

Our recent study had evaluated the effect of solvent polarity on the antioxidant potential of coconut waste [16]. This research therefore, seeks to further evaluate the effect of solvent polarity on the anticancer activity and the compounds responsible for their bioactivity.

2. Methodology

2.1 Sample Extract Preparation

The mesocarp (husk) was separated from the endocarp (shell) and washed to remove impurities prior to cutting it into smaller pieces. The collected husk and shell were sun dried and pulverized into a fine powder using grinder (Crusher D3V-10). The powder was kept in an airtight container and kept in a dark and cool place until analysis. Samples were extracted using six solvents of different polarity (methanol, propanol, ethyl acetate, acetone, chloroform and distilled water). 10 g of coconut shell and husk powder were extracted in 100 ml of each solvent of 70 % concentration. The extracts were incubated and agitated at 100 rpm for 48 hours. Then, the extracts were vacuum filtered and kept at 4 °C for analysis.

2.2 Cell Line and Culture Conditions

Breast cancer cell (MCF-7) used in these experiments were obtained from the Addexbio (San Diego, California, USA). The cells were cultured in MCF-7 cells complete medium (CM-0149) obtained from Elabscience, containing Minimum Essential Medium (MEM), 0.01 mg/ml insulin + 10 % Fetal Bovine Serum (FBS) + 1 % Penicillin-Streptomycin Solution (P/S). The cells were maintained at 37 °C under a humidified atmosphere of 95 % air and 5 % carbon dioxide (CO_2) and periodically screened for contamination.

2.3 Anticancer Activity by MTT Assay

The cell viability was assessed by metabolic reduction of 3-(4,5-dimetylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay (Sigma Aldrich, USA) by the mitochondrial succinate-*dehydrogenase* with slight modification [17–19]. The MCF-7 cells were seeded (4 × 104 cells per well) in a final volume of 100 µl/well in 96-well plates and incubated at 37 °C in a humidification incubator with 5 % CO_2 in complete medium. After 24 hours incubation, cells were treated with coconut husk and shell extracts of coconut at various concentrations (3, 5 and 10 mg/ml) for 24 hours. Then, 20 µl of 5 mg/ml of MTT dye in phosphate buffer saline (PBS) was added to the well and was left to be incubated for 4 hours. After the incubation the supernatant was removed and solubilized with dimethyl sulfoxide (DMSO) (100 µL). The MTT was then replaced by DMSO to dissolve formazan particles produced by viable cells. Afterwards, the plates were analyzed with ELISA reader at 570 nm. The cell viability was calculated using Eq. (1):

$$Cell\ Viabilty\ (\%) = \frac{A_{sample}}{A_{control}} \times 100\% \quad (1)$$

Where, A_{sample} is the absorbance of the sample extracts and $A_{control}$ is the absorbance of control.

2.4 Identification of Bioactive Compound by Gas Chromatography Mass Spectrometry (GCMS)

The chemical constituents of the extracts of coconut waste were identified by GCMS (Agilent 6890 series, China) equipped with a fused silica capillary column (30 m × 0.25 mm × 0.25 µm, coated by DB-5), with the EI operating at 70 eV. The injector temperature was set at 250°C. The oven temperature was programmed to hold at 40 °C for 1 min, thereafter, with an increase of 3 °C/min interval to 280 °C. Helium was used as the carrier gas (1 mL/min). The compounds were identified by

comparing the mass spectra with those in the National Institute of Standards and Technology (NIST) library [20].

2.5 Statistical Analysis

The analysis was performed in a triplicate manner. Results were expressed as mean standard deviation (SD) for each sample. Analysis of variance (ANOVA) and Dunnett's multiple comparisons test were used to determine significant differences between values ($p < 0.0001$) obtained for anticancer activity, with DMSO as the control. GraphPad Prism 9 version 9 for Windows was used for statistical analysis.

3. Results

3.1 Anticancer Activity

The selection of breast cancer as the focus of this research was based on its status as the most prevalent and lethal form of cancer among women, with no definitive medications available as of now [21-22]. Breast cancer is characterized by its heterogeneity, as some cases exhibit aggressive progression while others have a slow clinical course but a positive prognosis. This cancer ranks among the leading causes of cancer-related fatalities in women worldwide, with an annual incidence of 1.7 million cases. Projections suggest that by 2050, this figure will rise to around 3.2 million cases annually [23].

Biomass waste could potentially function as an abundant source of secondary metabolites endowed with anticancer attributes. The field of phytochemical investigation is presently garnering significant attention owing to the notable effectiveness of these compounds as anticancer agents, even at extremely low concentrations, while demonstrating minimal adverse impacts.

The effect different concentration of coconut shell and husk extracted using different polarity of solvent was tested against breast cancer cell line (MCF-7) by MTT assay. Results demonstrated that the cell viability of coconut shell and husk decreased as the extract concentration of increased. This result was in accordance with studies by [24], in which all solvents extract of thyme decreased the viability of f T47D breast cancer cell in a dose-dependent manner. Similar trends were also observed in the previous study of different solvent extracts of honeydew melon seed and whole fruit against PC3, HCT116, HeLa and Jurkat cell lines [25].

Figure 1 displayed that highest anticancer activity of coconut shell was exhibited by acetone extract at the highest concentration of 10 mg/ml; with only 65.20 ± 2.66 % of cell viability, indicating that 34.8 % of the cell was damaged. Meanwhile lowest cytotoxicity of 10.96 % was shown by chloroform extract at 3 mg/ml, which demonstrated the highest cell viability of 89.04 ±0.456 %. The results were similar to the study which reported that the acetone extract of all five Palestinian medicinal plants demonstrated the highest cytotoxicity as compared to the other extraction solvents used (90 % ethanol, 80 % methanol, coconut water, 5 % acetic acid, apple vinegar and grape vinegar) [26].

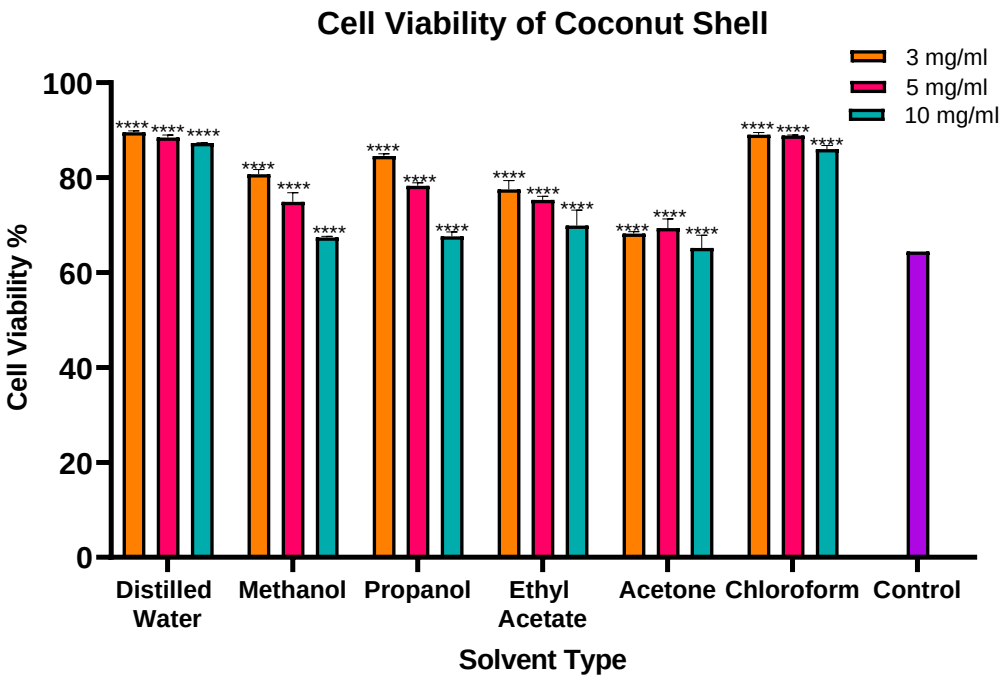

Fig. 1. Cell viability of coconut shell
****indicates $p < 0.0001$; when compared with DMSO as control

Figure 2 showed the cell viability of coconut husk using different polarity of solvent at different concentrations. Lowest cell viability was displayed by propanol extract at a concentration of 10 mg/ml (67.58 ± 2.48 %). Meanwhile highest cell viability was shown by methanol extract at 3 mg/ml concentration (87.89 ± 1.06 %). These results indicated that propanol extract of coconut husk exhibited the highest cytotoxicity (32.42 %) against MCF-7 and lowest cytotoxicity was demonstrated by methanol extract (12.11 %). From this result, despite methanol extract having a higher polarity compared to chloroform extract, the chloroform extract demonstrated a better cytotoxicity with only 85.40 ± 1.018 % cell alive, and 14.6 % were damaged at similar concentration.

Similar results were shown by Zhang *et al.,*[25], where chloroform extract of honeydew melon seed exhibited greater cytotoxicity against cervical cancer cells (Hela cell) line compared to methanol and distilled water extract. Studies by Khan *et al.,*[27], on the anticancer activity of *Artemisia judaica* also displayed similar result, where chloroform extract exhibited greater toxicity against human prostate cancer cell line (DU145) compared to their methanol extract.

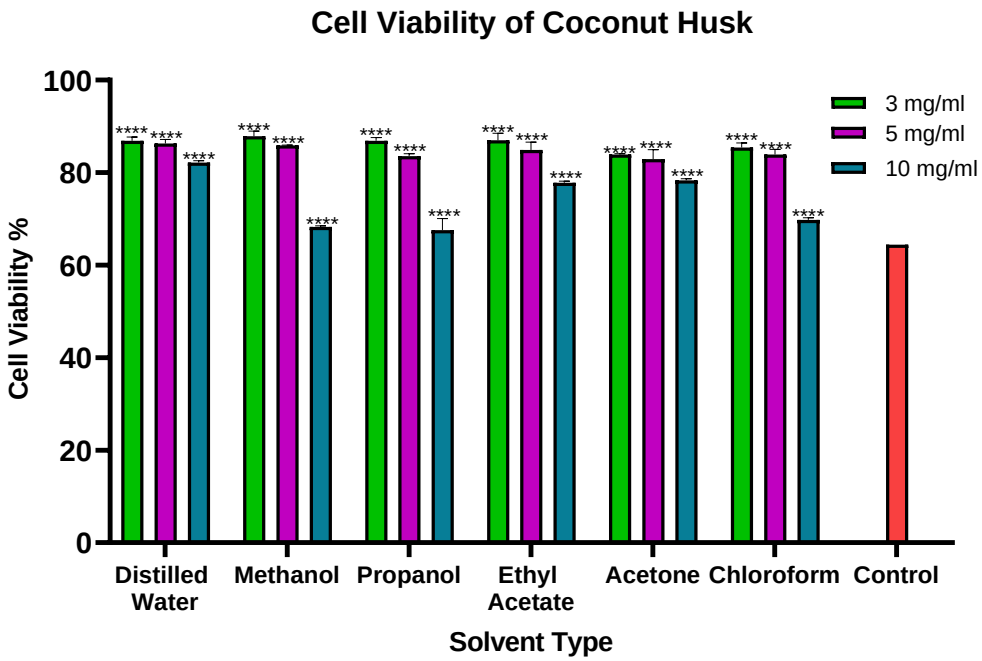

Fig. 2. Cell viability of coconut husk
****indicates $p < 0.0001$; when compared with DMSO as control

These results showed that the anticancer activity of coconut husk and shell is highly related to their antioxidant activity in our previous study where highest antioxidant activity was demonstrated by propanol extract and acetone of coconut husk and shell respectively [16]. This can be seen in the study by Darmadi *et al.,* [28] who reported that bioactive compounds are capable to inhibit the cancer growth by either activating apoptotic pathways involving mitochondria or death receptors. The study added that these compounds can function as agents that have both anti-aging and antioxidant properties, or act in both ways simultaneously. The presence of antioxidant activity is crucial for reducing oxidative stress and the formation of free radicals in the vicinity of cancerous environments.

3.2 Identification of Bioactive Compounds by GCMS

The data obtained from the GCMS analysis (Table 1) revealed that the major compounds in the acetone extract of coconut shell were dodecanoic acid (33.03 %), tetradecanoic acid (24.79 %), n-hexadeconoic acid (7.09 %) and (oxime-, methoxy-phenyl-(6.48 %). The compound was similar with Thebo *et al.,*[29] who discovered 13 saturated fatty acids including dodecanoic acid (0.89 %), n-Hexadecanoic acid (4.43 %), n-Octadecanoic acid (3.84 %) and tetradeconic acid (5.33 %). The greater antioxidant and anticancer activity of the acetone extract of coconut shell in this study may be attributed to its greater content of saturated fatty acid compared to the propanol shell extract.

Cyclic compounds such as phenol-2,4-Bis(1,1-Dimethylethyl) and cyclotrisiloxane,hexamethyl are unsaturated fatty acids and play a major role in the free radical scavenging, making them a promising antioxidant agent [30]. Both compounds were also found in acetone extract of *Turbinaria decurrens,* which were reported to be responsible for its antioxidant and antidiabetic activities [16].

In addition, the presence of 9,12-Octadecadienoic acid (Z, Z)- in the acetone extract of coconut shell may contribute to the antioxidant and anticancer activity of the extracts. 9,12-Octadecadienoic acid (Z, Z)-, is an essential unsaturated fatty acid found in mammalian nutrition and is used in biosynthesis of prostaglandins and cell membranes [31]. It was also reported to have anti-inflammatory hepatoprotective, antimicrobial, anticancer, anti-arthritic, anti-asthma and diuretic

activities [31]. Similar compounds were also found in the ethanolic crude extracts of the Libyan *Peganum harmala* [32], methanolic extracts of *Acmella uliginosa* [33] and in the essential oil of *C. winterianus* [31].

Table 1
Compounds identified from the major retention peaks obtained by GCMS analysis coconut shell acetone extract

Compound	Retention time	Area %	Molecular weight (g/mol)	Molecular formula
Isopropoxycarbamic acid, ethyl ester)	5.317	3.940	147.17	$C_6H_{13}NO_3$
Oxime-, methoxy-phenyl-_	10.185	6.480	151.16	$C_8H_9NO_2$
Biphenyl	29.875	1.300	154.2	$C_{12}H_{10}$
n-Decanoic acid	30.112	1.040	172.26	$C_{10}H_{20}O_2$
Benzaldehyde, 3-hydroxy-4-methoxy-	30.982	0.650	152.15	$C_8H_8O_3$
Phenol, 2,5-bis(1,1-dimethylethyl)	35.811	4.760	340.50	$C_{23}H_{32}O_2$
Dodecanoic acid	38.361	33.030	200.31	$C_{12}H_{24}O_2$
4-Hydroxy-2-methoxycinnamaldehyde	43.985	0.730	178.18	$C_{10}H_{10}O_3$
Tetradecanoic acid	45.4	24.790	228.37	$C_{14}H_{28}O_2$
n-Hexadecanoic acid	51.839	7.090	256.42	$C_{16}H_{32}O_2$
Dodecanoic acid, 2-hydroxy-1-(hydroxymethyl)ethyl ester	55.718	1.110	274.40	$C_{15}H_{30}O_4$
9,12-Octadecadienoic acid (Z, Z)-	56.987	1.610	280.45	$C_{18}H_{32}O_2$

For the coconut husk, the major components found in the propanol extract (Table 2) were Oxime-, methoxy-phenyl-(21.47 %), triterpenoid (13.50 %), 2,4-Di-tert-butylphenol (19.77 %), dibutyl phthalate (10.47 %) and Indole,3-methyl- (7.73 %).

Dibutyl phthalate was also discovered by [34], isolated from *Ipomoea carnea* stem using ethyl acetate and was reported to have a promising antimicrobial activity. 2,4-Di-tert-butylphenol was also found in chloroform whole fruit extract of honeydew melon [25]. Similarly, [35] highlighted the significant antioxidant activity of 2,4-Di-tert-butylphenol from sweet potato, which is relevant in the context of cancer prevention and treatment.

The excellent antioxidant and anticancer activity of the propanol extract compared to its acetone extract of the husk (Table 2) in this study may be contributed to the presence of indole, 3-methyl or skatole. This can be explained by [36], which suggested that small molecules produced by tryptophan metabolism such as skatole, can activate aromatic hydrocarbon receptors in different immune cells, suggesting its potential role in immune modulation and potentially in cancer immunotherapy.

Table 2
Compounds identified from the major retention peaks obtained by GCMS analysis of coconut husk propanol extract

Compound	Retention time	Area %	Molecular Weight (g/mol)	Molecular Formula
Isopropoxycarbamic acid, ethyl ester	5.982	6.400	147.17	$C_6H_{13}NO_3$
Cyclohexane, propyl-	9.326	5.510	126.24	C_9H_{18}
Oxime-, methoxy-phenyl-_	9.758	21.470	151.16	$C_8H_9NO_2$
2-Methyl-1-isopropyl(dimethyl)silyloxypropane	11.816	4.030	160.33	$C_8H_{20}OSi$
Indole, 3-methyl-	30.463	7.730	131.17	C_9H_9N
2,4-Di-tert-butylphenol	35.795	19.770	206.32	$C_{14}H_{22}O$
Dibutyl phthalate	51.499	10.740	278.34	$C_{16}H_{22}O_4$
Phenol, 2,2'-methylenebis[6-(1,1-dimethylethyl)-4-methyl-	64.896	6.260	340.499	$C_{23}H_{32}O_2$
Hexadecanoic acid, 2-hydroxy-1-(hydroxymethyl)ethyl ester	67.218	7.550	330.5	$C_{19}H_{38}O_4$

The GCMS data has confirmed that the antioxidant and anticancer activity does not solely depend on the phenolic compound but could be attributed by other factors such as fatty acid composition [37-38]. The extraction process is greatly influenced by the selection of a solvent with the appropriate polarity. It is possible for each secondary metabolite to interact with various plant components including proteins, lipids and carbohydrates. These interactions can lead to the formation of complexes that are challenging to dissolve. Furthermore, the solubility of compounds is also impacted by the polarity of the solvent used. These findings align well with the research conducted by [39], who demonstrated that different parts of the wood plant, which contain varying levels of secondary metabolites with specific polarities, necessitate extraction with solvents that possess suitable polarities.

4. Conclusions

In conclusion, the findings of this study demonstrated the promising potential of coconut waste, specifically its shell and husk, as a source of potent antioxidant and anticancer agents. The acetone extract of coconut shell exhibited the strongest anticancer activity, while the chloroform extract demonstrated the lowest cytotoxicity. Similarly, the propanol extract of coconut husk displayed the highest cytotoxicity against MCF-7 cells, whereas the methanol extract showed the lowest. These results highlight the varying biological activities within different extracts of coconut waste.

Furthermore, GCMS analysis identified key compounds in both coconut shell and husk, including dodecanoic acid, tetradecanoic acid and oleic acid, which are known to possess antioxidant and anticancer properties. The presence of these compounds provides a scientific basis for the observed biological activities of the coconut waste extracts. Overall, this research supports the exploration of coconut waste as a valuable resource for developing novel therapeutic interventions for oxidative stress-related diseases and cancer. Further investigations into the specific mechanisms of action of the identified compounds and their potential synergistic effects are warranted to fully realize the therapeutic potential of coconut waste.

Acknowledgement
This research was funded by Malaysia Japan International Institute of Technology Incentive.

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