Tropical Journal of Pharmaceutical Research March 2025; 24 (3): 311-321
ISSN: 1596-5996 (print); 1596-9827 (electronic)

Available online at http://www.tjpr.org
http://dx.doi.org/10.4314/tjpr.v24i3.3

Original Research Article

Impact of palmitic acid-enriched supplement on pancreatic cancer (PANC-1) and its antimicrobial potential

Nahed Ahmed Hussien[1]*, Ehab M Tantawy[2]
[1]Department of Biology, College of Science, Taif University, Taif 21944, Saudi Arabia, [2]Research and Development Sector, EGYVAC, VACSERA, Giza 12311, Egypt

For correspondence:* ***Email:* *n.nahed@tu.edu.sa*

Sent for review: 17 December 2024 *Revised accepted: 12 March 2025*

Abstract

Purpose: *To investigate the anti-pancreatic cancer and antimicrobial effects of fat-enriched dietary supplements (FEDS).*
Method: *Gas chromatography-mass spectrometry (GC-MS) was used to screen FEDS components. The FEDS cytotoxicity (SRB) was assessed using mouse endothelial (non-cancerous, C-166 normal cells) and pancreatic cancer line (PANC-1). Antimicrobial evaluation of FEDS was conducted against different microbial strains to obtain the minimum inhibitory (MIC) and bactericidal (MBC) concentrations.*
Results: *Gas chromatography-mass spectrometry (GC-MS) revealed that the predominant fatty acid found in the present supplement is palmitic acid (< 75 %), followed by α-linoleic acid (7.39 %), stearic acid (5.76 %), and other polyunsaturated fatty acids (≤ 2 %). The FEDS exhibited a dose-dependent, low cytotoxic effect (0.001 -100 µg/mL) against PANC-1 pancreatic cancer cells (IC_{50} > 100 µg/mL) and C-166 (IC_{50} = 164.71). A high PA-palmitic acid-enriched supplement shows antifungal and mild antibacterial potential against common strains that contribute to pancreatic cancer development. Candida albicans, Gram-positive (Bacillus cereus, Enterococcus faecalis, and Staphylococcus aureus), and Gram-negative (Escherichia coli) strains showed MIC and MBC > 1000 µg/mL.*
Conclusion: *This finding highlights the complex interplay between dietary fats, cytotoxicity, and antimicrobial activity in pancreatic cancer. Future studies should focus on the specific roles of different fatty acids and their interactions with the tumor microenvironment to develop targeted nutritional strategies that may improve survival and quality of life for individuals affected by pancreatic ductal adenocarcinoma (PDA).*

Keywords: *Palmitic acid, PANC-1, Pancreatic cancer, C-166, Antimicrobial, Cytotoxicity*

Tropical Journal of Pharmaceutical Research is indexed by Scopus, Chemical Abstracts, Embase, Index Copernicus, EBSCO, African Index Medicus, JournalSeek, Directory of Open Access Journals (DOAJ), African Journal Online, Bioline International, Open-J-Gate and Pharmacy Abstracts.

INTRODUCTION

Pancreatic ductal adenocarcinoma (PDA) is the most common and deadly type of pancreatic cancer. About 90 % of patients die within 5 years of diagnosis. The low survival rate is due to the aggressive nature of the disease, lack of early detection tools, and limited understanding of its causes [1,2]. Possible explanations for the rise in pancreatic cancer incidence include increased tobacco use, diabetes, obesity, physical inactivity, and diets that are high in calories and fats [3]. Improved clinical recognition and diagnosis of pancreatic cancer and increasing life expectancy may also contribute to global incidence rise [4]. Nutrition is vital for cancer treatment outcomes, yet malnutrition affects 50 % of patients and is

often overlooked [5]. Cancer patients often face changes in body composition and nutritional deficiencies, with up to 51 % having nutritional deficiencies and 9 % being overtly malnourished [6]. This leads to impairments in physical function and decreased survival [5]. Malnutrition in pancreatic cancer patients results in muscle loss, fat breakdown, extended hospital stays, heightened complications, diminished treatment effectiveness, reduced survival rates, lower quality of life, and increased morbidity and mortality. If a patient's oral intake is inadequate to maintain their body weight and composition, additional nutritional therapy becomes imperative [7].

Concomitant management of fat malabsorption and malnutrition is fundamental in treating PDA [8]. There is a controversy regarding the impact of dietary fat composition on pancreatic cancer incidence, progression, and metastasis. Several studies indicated that diets rich in omega-3 polyunsaturated fatty acids are linked to a lower risk of pancreatic cancer. However, there is currently insufficient evidence to draw a definitive conclusion about the influence of other types of fat on pancreatic cancer development, as many studies have produced inconclusive results due to limitations in design [9].

Studies have indicated that the interactions of microorganisms, whether close to or distant from tumor tissues, influence cancer progression. Each type of tumor has a unique microbiome composition, with a majority of bacteria located within cancer and immune cells [10]. This is also true for pancreatic cancer. Recent studies implied that bacteria could be involved in various gastrointestinal cancers. Specific bacterial ecosystems found in pancreatic cyst fluid may mirror the local microbiota present in the pancreas. In contrast to healthy pancreatic tissue, pancreatic cancer tissue contains a diverse array of microorganisms, including bacteria and fungi, which not only support the development of pancreatic cancer but also affect its response to treatment [11]. This study investigated the impact of fat-enriched dietary supplements (FEDS) on pancreatic cancer cells and their antimicrobial potential. Chromatography-mass spectrometry (GC-MS) was used to screen FEDS' main components for cytotoxicity against non-cancerous mouse endothelial (C-166) cells.

EXPERIMENTAL

Preliminary compound screening

Fat-enriched dietary supplement (FEDS) capsules were purchased from local stores and stored in dry and cool conditions before further evaluation. An RTX-5 MS capillary column from Restek was employed to chemically characterize the FEDS (95 % methanolic extract) using a GC-MS-QP2010 Plus system from Shimadzu, Japan. The GC separates the different constituents based on their variable retention times (RT), while the mass spectrophotometer identifies these components. The software linked to the mass spectrophotometer generates a chromatogram showing the relative abundance against RT. The obtained spectra were compared with the spectra of unknown compounds with the Wiley Registry8e library for easy identification and chemical characterization.

In vitro cytotoxicity evaluation

Mouse endothelial (non-cancerous, C-166) and pancreatic cancer (PANC-1) cell lines were provided by Nawah Scientific Inc., Mokatam, Cairo, Egypt. The C-166 cells were maintained in Dulbecco's Modified Eagle's Medium (DMEM), while the PANC-1 cells were maintained in Roswell Park Memorial Institute medium (RPMI-1640), under 10 % heat-inactivated fetal bovine serum (FBS), and penicillin–streptomycin (100 U/mL). The cells were incubated at 37 ℃ in a humid environment (5 % carbon dioxide (CO_2)). Aliquots of cell suspension (100 µL) were incubated in media (DMEM/RPMI-1640 for C-166/PANC-1 cells) in 96-well plates for 24 h. Cells were treated with 100 µL/well FEDS (0.001-100 µg/mL in DMEM/RPMI-1640 media for C-166/PANC-1 cells). Following FEDS treatment, 150 µL of trichloroacetic acid (TCA at a concentration of 10 % in media was introduced to the treated cells. They were then incubated at 4 °C for 1 h to facilitate cell fixation. After TCA removal and washing, cells were treated with Sulforhodamine B solution (SRB, 70 µL/well, 0.4 %w/v) for 10 min in a dark place. The cells were washed three times with 1 % acetic acid solution and allowed to air dry overnight. Subsequently, a 150 µL tris base solution was added (pH 10.5, 10 mM) per well. The absorbance was then measured at 540 nm using an Infinite F50 microplate reader (TECAN, Switzerland). The percentage cell viability (V) was determined according to Eq 1 and then plotted for IC_{50} (50 % inhibition concentration) assessment [12].

$V (\%) = (A_F/A_c)100$ …… (1)

Where A_F is the mean absorbance of FEDS and A_c is mean absorbance of control

Antimicrobial evaluation

The present study utilizes four bacterial strains (*Escherichia coli* ATCC 8739, *Staphylococcus aureus* ATCC 29213, *Enterococcus faecalis* ATCC 19433, and *Bacillus cereus* ATCC 9634) and one fungus (*Candida albicans* ATCC 10231) obtained from Nawah Scientific Inc., Mokatam, Cairo, Egypt. Different strains were introduced into a tryptic soy broth medium and incubated at 37 °C for 24 h. A small amount of broth was then spread onto tryptic soy agar and placed in the 37 °C incubator for 18-24 h to create a fresh culture on the agar plate. A sterile saline solution was prepared by selecting 3 to 4 colonies from the agar plate. This solution was then adjusted to 0.5 McFarland standard for each strain and diluted with sterile Mueller-Hinton broth (MHB) to achieve a concentration of approximately 1.0×10^6 CFU/mL. For each bacterial strain treatment, two-fold FEDS dilutions (1000 to 1.953 µg/mL) were used. Negative and positive (using ciprofloxacin antibiotic at serial dilution 1000 - 1.953 µg/mL) controls were included. The minimum bactericidal concentration (MBC) and minimum inhibitory concentration (MIC) of FEDS were assessed against various strains [13].

RESULTS

Chromatogram of the fat-enriched supplement (FEDS) had a higher peak at 28.17 retention time (RT; Figure 1).

Characterization of components

The main fatty acid reported in the present supplement was palmitic acid (a saturated fatty acid (SFA) at 28.17 RT, followed by α-linoleic acid (7.39 %, polyunsaturated (PUFA), stearic acid (5.76%, SFA), and a low amount of other PUFAs (≤ 2 %; Table 1 to Table 4).

Cytotoxic effect

Fat-enriched dietary supplement (FEDS) demonstrated a dose-dependent cytotoxic effect (0.001 - 100 µg/mL) against non-cancerous mouse endothelial (C-166) and pancreatic cancer (PANC-1) cell lines (Figures 2 and 3). Palmitic acid-based supplements decreased pancreatic cancerous cell (PANC-1) viability with an IC_{50} > 100 µg/mL, higher than non-cancerous cells (C-166; Figure 3).

Antimicrobial activity

The minimum inhibitory concentration (MIC) and minimum bactericidal concentration of the FEDS were greater than 1000 µg/mL (Table 5).

DISCUSSION

Chromatography-mass spectrometry (GC-MS) is an effective technique for characterizing constituents. It is cost-effective with high sensitivity compared to other techniques. This makes it widely useful in food analysis, especially for determining volatile organic compounds and performing qualitative and quantitative analyses of various compounds [14]. Different fatty acids were identified and quantified using a GC-MS technique. The main fatty acid reported in this study was palmitic acid (more than 75 %). The GC-MS technique is a highly selective and sensitive method for analyzing components in dietary supplements prevalent in today's health-conscious society [15].

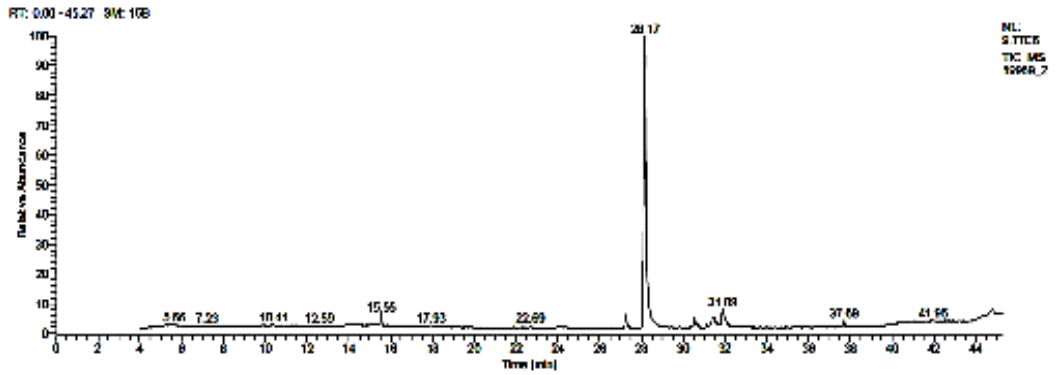


Figure 1: Chromatogram of the fat-enriched supplement used in the present study

Table 1: Components found in supplement of the present study

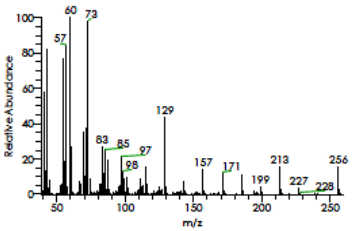
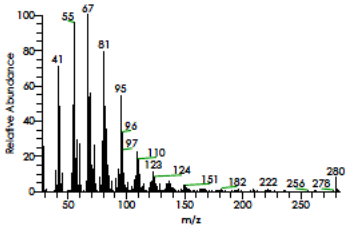
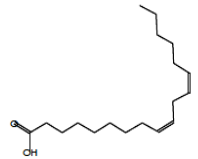
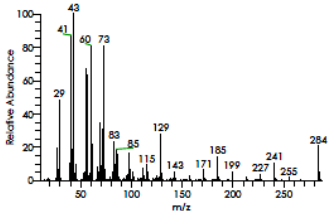
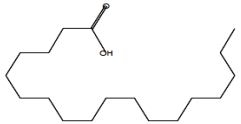
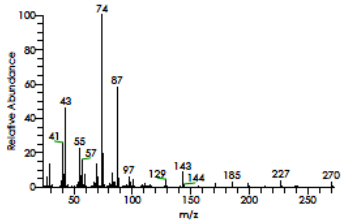
Compound name	Retention time, RT (min)	Area (%)	Molecular formula	Mass spectrum	Structure
n-Hexadecanoic acid (Palmitic acid)	28.17	73.59	$C_{16}H_{32}O_2$		
9,12-Octadecadienoic acid (Z,Z)- (α-Linoleic acid)	31.89	7.39	$C_{18}H_{32}O_2$		
Octadecanoic acid (Stearic acid)	31.42	5.76	$C_{18}H_{36}O_2$		
Pentadecanoic acid, 14-methyl-, methyl ester	27.24	3.21	$C_{17}H_{34}O_2$		

Table 2: Components found in supplement of the present study *(continued A)*

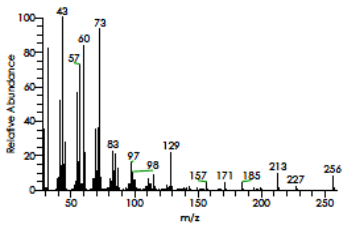
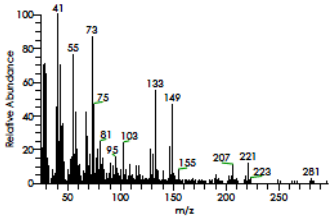
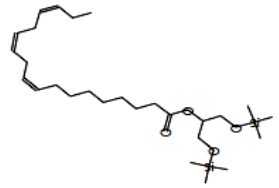
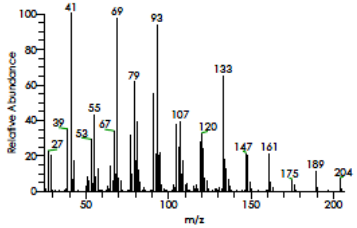
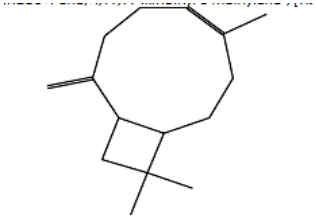
Compound name	Retention time, RT (min)	Area (%)	Molecular formula	Mass spectrum	Structure
n-Hexadecanoic acid (Palmitic acid)	28.60	2.85	$C_{16}H_{32}O_2$		
9,12,15-Octadecatrienoic Acid, 2-{(Trimethylsilyl)Oxy}-1-{{(Trimethylsilyl)Oxy}MethyL}Ethyl Ester, (Z, Z, Z)-	44.77	2.16	$C_{27}H_{52}O_4Si_2$		
Caryophyllene	15.56	2.05	$C_{15}H_{24}$		

Table 3: Components found in supplement of the present study *(continued B)*

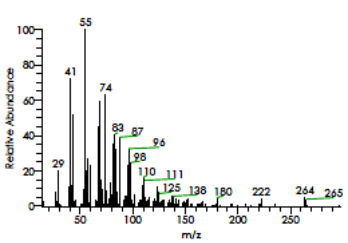
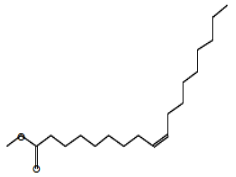
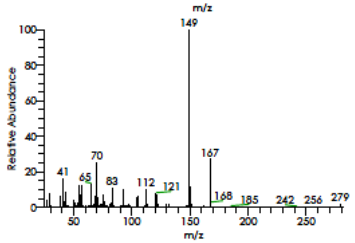
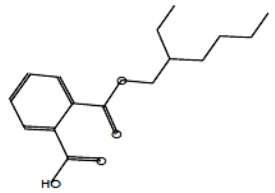
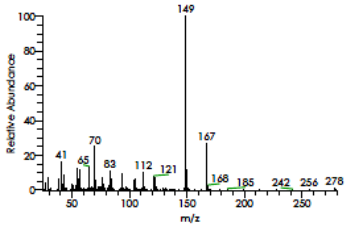
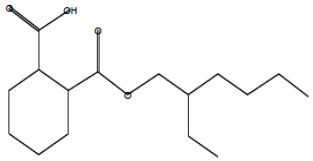
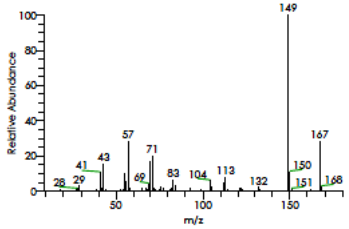
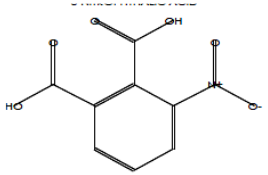
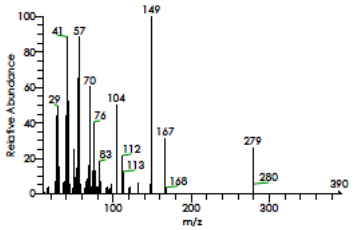
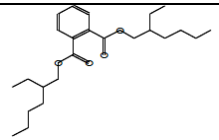
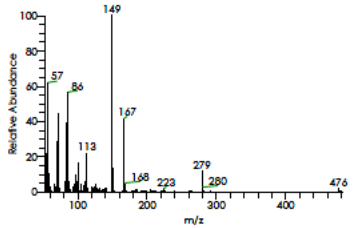
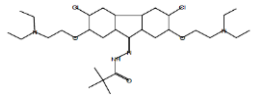
Compound name	Retention time, RT (min)	Area (%)	Molecular formula	Mass spectrum	Structure
9-Octadecenoic acid (Z)-, methyl Ester (Methyl oleate)	30.54	1.85	$C_{19}H_{36}O_2$		
2-({(2-Ethylhexyl)Oxy}Carbo Nyl)Benzoic Acid	37.69	1.13	$C_{16}H_{22}O_4$		
Mono(2-ethylhexyl) phthalate	37.69	1.13	$C_{16}H_{22}O_4$		
1,2-Benzenedicarboxylic Acid, 3-Nitro-	37.69	1.13	$C_8H_5NO_6$		

Table 4: Components found in supplement of the present study *(continued C)*

Compound name	Retention time, RT (min)	Area (%)	Molecular formula	Mass spectrum	Structure
1,2-Benzenedicarboxylic Acid (Phthalic acid)	37.69	1.13	$C_{24}H_{38}O_4$		
9-(2',2'-Dimethylpropanoilhydrazono)-3,6-dichloro-2,7-bis-{2-(diethylamino)-ethoxy}fluorene	37.69	1.13	$C_{30}H_{42}Cl_2N_4O_3$		

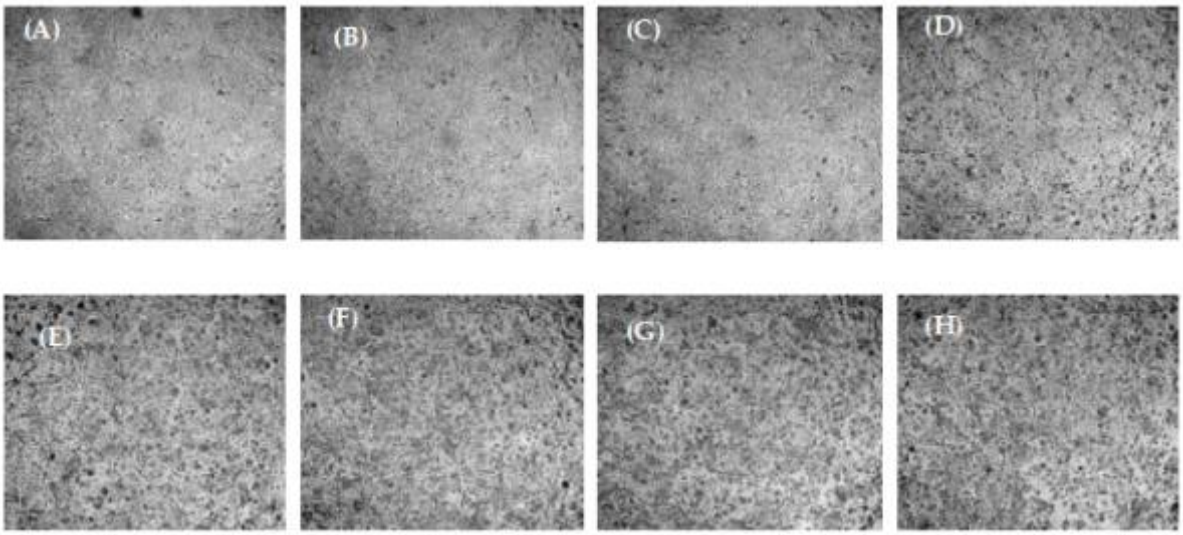


Figure 2: Morphological representation of mouse endothelial, C-166 (A-D), and pancreatic cancer PANC-1 (E-H) cells treated by various concentrations (0, 1, 10, 100 µg/mL) of palmitic acid-based supplement

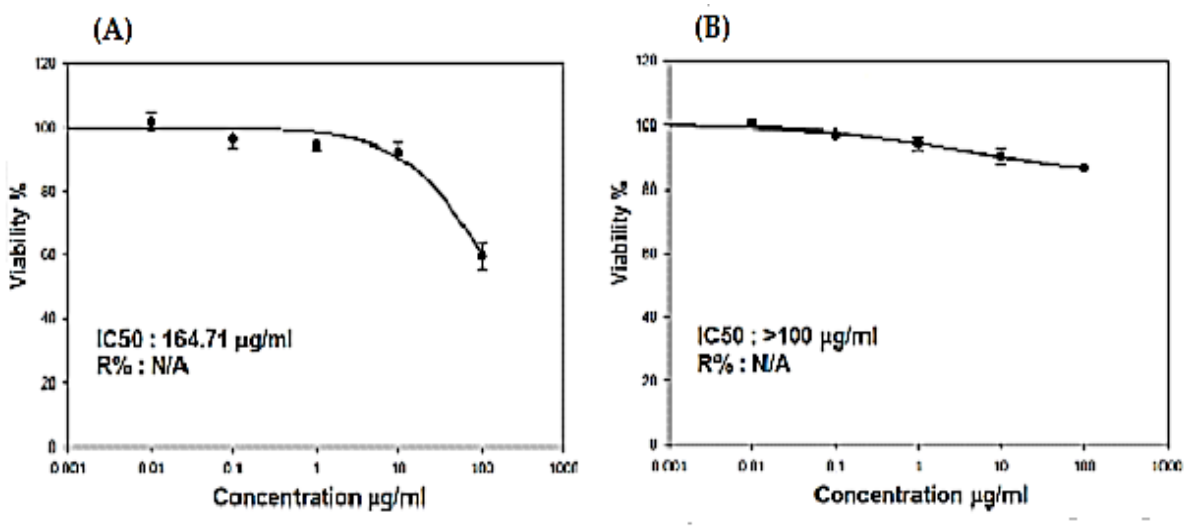


Figure 3: Cell viability percentage of non-cancerous mouse endothelial C-166 (A) and pancreatic cancer PANC-1 (B) cells treated with palmitic acid-enriched supplement

Table 5: MIC and MBC of FEDS

Bacterial strain	(FEDS µg/mL)	
	b	***MBC***
Bacillus cereus	>1000	>1000
Candida albicans	>1000	>1000
Enterococcus faecalis	>1000	>1000
Escherichia coli	>1000	>1000
Staphylococcus aureus	>1000	>1000

Fat-enriched dietary supplement (FEDS) demonstrated a dose-dependent cytotoxic effect (0.001 - 100 µg/mL) against non-cancerous mouse endothelial (C-166) and pancreatic cancer (PANC-1) cell lines. However, cytotoxicity was observed in non-cancerous C-166 cells, with a lower IC_{50} compared to cancerous pancreatic cells (PANC-1).

Excessive amount of free fatty acids (FFAs) leads to cellular toxicity, a condition known as lipotoxicity [16]. High content of palmitic acid (PA) in FEDS may be the primary fatty acid responsible for the observed cytotoxicity. Palmitic acid, the most prevalent saturated fatty acid found in the bloodstream [17], has been shown to cause apoptotic cell death in various cells. Previous studies showed that treatment with PA caused

G2/M arrest, increased reactive oxygen species (ROS) production, and elevated levels of endoplasmic reticulum stress-related proteins [18]. Excessive PA accumulation in microglial cells leads to lipotoxicity, resulting in decreased cell viability and increased cell death. These are mediated by intracellular mechanisms rather than cell surface receptors [19]. A recent study reported that PA treatment for 4 h does not affect cell viability but increases ROS and NO production in human vascular endothelial cells (HUVECs) [20].

Evidence suggests that various lipids, including fatty acids, may have anticancer effect acting at the mitochondrial level [18]. Findings from this study revealed that palmitic acid-based supplement decreases pancreatic cancerous cell (PANC-1) viability with an IC_{50} higher than non-cancerous cells (C-166). At higher concentrations, the cells gradually became more rounded and exhibited decreased cell-to-cell contact, a typical feature of cellular death. Palmitic acid (PA, C16:0) which is the most common saturated fatty acid in the human diet has been studied as a potential anti-tumor agent against various malignancies [21]. Palmitic acid triggers apoptosis in cancer cells via the mitochondrial pathway, increases reactive oxygen species (ROS) levels within the cells, and leads to programmed autophagic cell death and cell cycle arrest. Additionally, it inhibits cell migration, invasion, and angiogenesis, enhancing effectiveness of chemotherapy while targeting critical pathways involved in cancer cell behavior [21].

This current study indicated that a palmitic acid-based supplement has a greater cytotoxic effect on normal cells compared to pancreatic cancer cell lines. However, the potential of palmitic acid against pancreatic cancer remains a topic of debate. Palmitic acid stimulates pancreatic cancer AsPC-1 cells by inducing TLR4-mediated cell invasion, leading to ROS generation, activation of nuclear factor-kappa beta (NF-Kβ), secretion and activation of MMP-9, associated with increased cancer metastatic potential [22]. Earlier studies reported that PA conjugated with triphenylphosphonium, a lipophilic cationic moiety, reduces proliferation of pancreatic cancerous PANC-1 parental (P) cells and pancreatic cancer stem cells (PCSCs) with IC_{50} values of 31 and 18 µM, respectively [23]. This suppression was through mitochondrial disruption, leading to ROS increase, ER stress activation, and cell autophagy. While there are conflicting findings regarding PA's effects on pancreatic cancer cells, further studies are needed to fully understand its impact and potential applications in cancer treatment. The dual nature of the effect of palmitic acid on different cancer cell lines underscores the complexity of its interactions within the cellular environment. Further studies are required to elucidate the mechanisms underlying these contrasting effects and to determine the conditions under which PA may be beneficial in combating pancreatic cancer.

The human microbiome is now being studied as a new target for understanding cancer development. Recent studies suggest that the specific bacterial community found in pancreatic cyst fluid may indicate the local microbiota in the pancreas. Microorganisms in pancreatic cancer tissue contribute to cancer development and affect treatment response and prognosis [24]. Therefore, different bacterial and fungal (*Bacillus cereus, Candida albicans, Enterococcus faecalis, Escherichia coli, and Staphylococcus aureus*) strains were targeted to determine the antimicrobial potential of FEDS. There is a relation between the colonization of those selected strains in a specific tissue and cancer invasion. Targeting microbial infection could be a new approach to treat cancer, including pancreatic cancer. Certain fungi (including *Candida albicans*) migrating from the intestine to colonize the pancreas are linked to pancreatic cancer [25]. *Candida* produces nitrosamines, which are carcinogens that promote cancer through a proinflammatory response, increasing cytokine production and expression of adhesion molecules. *Enterococcus faecalis* has been found in the pancreatic tissue of patients with chronic pancreatitis and pancreatic cancer, while bile microbiota, such as *Escherichia coli*, may affect pancreatic microbiota [25,26]. Few bacteria may migrate from the gallbladder to the pancreas, and their clearance may trigger a protective immune response against pancreatic cancer [27]. A high PA-enriched supplement (FEDS) shows antifungal potential against *Candida albicans* which is consistent with previous study [28]. Treatment with PA induces apoptosis in *Candida* species by causing mitochondrial dysfunction through the production of reactive oxygen species (ROS). In addition, PA-enriched supplement (FEDS) exhibited mild antibacterial effects against Gram-positive (*Bacillus cereus, Enterococcus faecalis, and Staphylococcus aureus*) and Gram-negative (*Escherichia coli*) strains with MIC and MBC >1000 µg/mL.

Palmitic acid, either in nanostructured or encapsulated in liposome carriers, shows antibacterial properties against *Pseudomonas aeruginosa* and *S. aureus* [29], multidrug-resistant *Staphylococcus epidermidis*, and Vancomycin-resistant *Enterococcus faecalis* [30]. The reason for the higher potency of PA in previous studies

compared to this study is that drug carriers such as liposomes were used to facilitate drug delivery. High concentrations of PA increase cellular toxicity and the rate of cell death, while also affecting microbial virulence through antibiofilm activity and reactive oxygen species (ROS) production, which lead to significant DNA, RNA, and protein damage [28,31].

CONCLUSION

Fat-enriched dietary supplement (FEDS), particularly those high in palmitic acid, exhibits mild cytotoxic effects on normal and pancreatic cancer cell lines with antimicrobial properties against various pathogenic strains. Future studies should focus on the specific roles of different fatty acids and their interactions with the tumor microenvironment to develop targeted nutritional strategies that may improve survival and quality of life for individuals affected by PDA.

DECLARATIONS

Acknowledgement/Funding

The authors would like to acknowledge the Deanship of Graduate Studies and Scientific Research, Taif University for funding this work.

Ethical approval

None required.

Use of Artificial intelligence/Large language models

We also declare that we did not use Generative artificial intelligence (AI) and AI-assisted technologies in writing the manuscript.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Conflict of interest

No conflict of interest is associated with this work.

Contribution of authors

We declare that this work was done by the author(s) named in this article, and all liabilities pertaining to claims relating to the content of this article will be borne by the authors.

REFERENCES

1. *Siegel RL, Miller KD, Jemal A. Cancer statistics. CA Cancer J Clin 2020; 70: 7–30.*
2. *Liu L, Chen L, Yang J, Ye C, Yang P, Zhang LF, Shen B. LZTS1 promotes proliferation and suppresses apoptosis by inhibiting the activation of AKT/GSK-3β signaling pathway in pancreatic cancer cells. Trop J Pharm Res 2022; 21: 31-36.*
3. *Larsson SC, Permert J, Håkansson N, Näslund I, Bergkvist L, Wolk A. Overall obesity, abdominal adiposity, diabetes and cigarette smoking in relation to the risk of pancreatic cancer in two Swedish population-based cohorts. Br J Cancer 2005; 93: 1310–1315.*
4. *Khalaf N, El-Serag HB, Abrams HR, Thrift AP. Burden of pancreatic cancer: from epidemiology to practice. Clin Gastroenterol Hepatol 2021; 19: 876–884.*
5. *Azzini E, Furini T, Polito A, Scalfi L, Pinto A, Gasperi V, Savini I. On behalf of the SINU "Nutrition in Oncology" Working Group. Vitamin nutritional status in patients with pancreatic cancer. A narrative review. Int J Mol Sci 2024; 25: 4773.*
6. *Muscaritoli M, Lucia S, Farcomeni A, Lorusso V, Saracino V, Barone C, Plastino F, Gori S, Magarotto R, Carteni G, et al. Prevalence of malnutrition in patients at first medical oncology visit: The PreMiO study. Oncotarget 2017; 8: 79884–79896.*
7. *Fearon KCH, Baracos VE. Cachexia in pancreatic cancer: new treatment options and measures of success. HPB (Oxford) 2010; 12: 323-324.*
8. *Carrato A, Cerezo L, Feliu J, Macarulla T, Martín-Pérez E, Vera R, Álvarez J, Botella-Carretero JI. Clinical nutrition as part of the treatment pathway of pancreatic cancer patients: an expert consensus. Clin Transl Oncol 2022; 24(1): 112-126.*
9. *Wirkus J, Ead AS, Mackenzie GG. Impact of dietary fat composition and quantity in pancreatic carcinogenesis: Recent advances and controversies. Nutrition research (New York) 2021; 88: 1–18.*
10. *Nejman D, Livyatan I, Fuks G, Gavert N, Zwang Y, Geller LT, Rotter-Maskowitz A, Weiser R, Mallel G, Gigi E, et al. The human tumor microbiome is composed of tumor-type-specific intracellular bacteria. Sci 2020; 368: 973–980.*
11. *Li S, Fuhler GM, Bn N, Jose T, Bruno MJ, Peppelenbosch MP, Konstantinov SR: Pancreatic cyst fluid harbors a unique microbiome. Microbiome 2017; 5: 147.*
12. *Allam RM, Al-Abd AM, Khedr A, Sharaf OA. Fingolimod interrupts the cross-talk between estrogen metabolism and sphingolipid metabolism within prostate cancer cells. Toxicol Lett 2018; 291: 77-85.*
13. *European Committee for Antimicrobial Susceptibility Testing (EUCAST) of the European Society of Clinical Microbiology and Infectious Diseases (ESCMID). Determination of minimum inhibitory concentrations (MICs) of antibacterial agents by broth dilution. Clin Microbiol Infect 2003; 9: ix-xv.*

14. Brotas MSC, Carvalho GA, Pereira PAP. Determination, through derivatization and GC-MS analysis, of Omega-3 and Omega-6 fatty acids in fish oil capsules sold in Salvador, Bahia. J Braz Chem Soc 2020; 31: 447–455.
15. Samanta K, Nath P, Patel R, Singh G, Jain A, Nandi G. Advances of GC-MS in the determination of adulterants in dietary supplements. E3S Web Conf 2024; 556: 01053.
16. Malhi H, Gores GJ. Molecular mechanisms of lipotoxicity in nonalcoholic fatty liver disease. Semin Liver Dis 2008; 28: 360–369.
17. Abdelmagid SA, Clarke SE, Nielsen DE, Badawi A, El-Sohemy A, Mutch DM, Ma DW. Comprehensive profiling of plasma fatty acid concentrations in young healthy Canadian adults. PLoS ONE 2015; 10: e0116195.
18. Park EJ, Lee AY, Park S, Kim JH, Cho MH. Multiple pathways are involved in palmitic acid-induced toxicity. Food Chem Toxicol Int J Publ Br Ind Biol Res Assoc 2014; 67: 26–34.
19. Urso CJ, Zhou H. Palmitic acid lipotoxicity in microglia cells is ameliorated by unsaturated fatty acids. Int J Mol Sci 2021; 22: 9093.
20. Choroszy M, Środa-Pomianek K, Wawrzyńska M, Chmielarz M, Bożemska E, Sobieszczańska B. The role of palmitic acid in the co-toxicity of bacterial metabolites to endothelial cells. Vasc Health Risk Manag 2023; 19: 399–409.
21. Wang X, Zhang C, Bao N. Molecular mechanism of palmitic acid and its derivatives in tumor progression. Front Oncol 2023; 13: 1224125.
22. Binker-Cosen MJ, Richards D, Oliver B, Gaisano HY, Binker MG, Cosen-Binker LI. Palmitic acid increases invasiveness of pancreatic cancer cells, AsPC-1, through TLR4/ROS/NF-κB/MMP-9 signaling pathway. Biochem Biophys Res Commun 2017; 484(1): 152–158.
23. Siragusa G, Brandi J, Rawling T, Murray M, Cecconi D. Triphenylphosphonium-conjugated palmitic acid for mitochondrial targeting of pancreatic cancer cells: proteomic and molecular evidence. Int J Mol Sci 2024; 25: 6790.
24. Pushalkar S, Hundeyin M, Daley D, Zambirinis CP, Kurz E, Mishra A, Mohan N, Aykut B, Usyk M, Torres LE, et al. The pancreatic cancer microbiome promotes oncogenesis by induction of innate and adaptive immune 452 suppression. Cancer Discov 2018; 8: 403–416.
25. Chung LM, Liang JA, Lin CL, Sun LM, Kao CH. Cancer risk in patients with candidiasis: a nationwide population-based cohort study. Oncotarget 2017; 8(38): 63562–63573.
26. Maekawa T, Fukaya R, Takamatsu S, Itoyama S, Fukuoka T, Yamada M, Hata T, Nagaoka S, Kawamoto K, Eguchi H, et al. Possible involvement of Enterococcus infection in the pathogenesis of chronic pancreatitis and cancer. Biochem Biophys Res Commun 2018; 506: 962–969.
27. Archibugi L, Signoretti M, Capurso G. The microbiome and pancreatic cancer: an evidence-based association? J Clin Gastroenterol 2018: S82–85.
28. Prasath KG, Tharani H, Kumar MS, Pandian SK. Palmitic acid inhibits the virulence factors of Candida tropicalis: biofilms, cell surface hydrophobicity, ergosterol biosynthesis, and enzymatic activity. Front Microbiol 2020; 11: 864.
29. Ivanova E, Nguyen S, Guo Y, Baulin V, Webb H, Truong V, Wandiyanto JV, Garvey CJ, Mahon PJ, Mainwaring DE, et al. Bactericidal activity of self-assembled palmitic and stearic fatty acid crystals on highly ordered pyrolytic graphite. Acta Biomaterialia 2017; 59: 148–157.
30. Cheung Lam A, Sandoval N, Wadhwa R, Gilkes J, Do T, Ernst W, Chiang SM, Kosina S, Howard Xu H, Fujii G, et al. Assessment of free fatty acids and cholesteryl esters delivered in liposomes as a novel class of antibiotic. BMC Res Notes 2016; 9: 337.
31. Ray PD, Huang BW, Tsuji Y. Reactive oxygen species (ROS) homeostasis and redox regulation in cellular signaling. Cell Signal 2012; 24: 981–990.