Nutrição e promoção da saúde:

Perspectivas atuais

Anne Karynne da Silva Barbosa
(Organizadora)

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Nutrição e promoção da saúde: perspectivas atuais

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APRESENTAÇÃO

A coleção “Nutrição e Promoção da Saúde: perspectivas atuais” é um conjunto que possui principal objetivo de incorporar pesquisas resultantes de trabalhos em diversas áreas que integram a Nutrição. Esse volume aborda de forma interdisciplinar com artigos, pesquisas, relatos de experiência e/ou revisões da literatura.

A principal característica desse volume, foi partilhar de forma simples e clara os trabalhos desenvolvidos em diversas instituições de ensino e pesquisa de graduação e pós-graduação do país. Nestes artigos que foram selecionados a partir de revisão, a linha basal foi o aspecto relacionado com as diversas áreas que compõe nutrição e suas áreas correlatas.

Temas considerados relevantes sobre a área de nutrição e da saúde são partilhados aqui com o intuito de contribuir com o conhecimento de alunos, promover a troca de experiências de docentes entre as diversas instituições e aumentar o aprendizado de todos aqueles que se interessam pela saúde e pela pesquisa na área de nutrição. Visto que, esse volume traz pesquisas atuais, com muitas temáticas que irão apoiar a prática clínica de profissionais nutricionistas e os da área da saúde em geral.

Portanto, aqui se traz o resultado de inúmeros trabalhos, fundamentados em parte na teoria e parte na prática, produzidos e compartilhados por professores e alunos. Sabe-se a importância de uma divulgação adequada da literatura científica, por isso a melhor escolha foi a Atena Editora, posto que possui uma plataforma didática e relevante para todos os pesquisadores que queiram compartilhar os resultados de seus estudos.

Boa leitura!

Anne Karynne da Silva Barbosa

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POTENTIAL FOR THE TREATMENT OF CANCER FROM AGRO-INDUSTRIAL RESIDUES - A REVIEW

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ABSTRACT: With the constant increase in global urbanization, the profile of food consumption and the potential for chronic diseases such as cancer have been changing. Supplying overpopulation is the role of the food industry, which aims to meet this demand, increasing, in recent years, the generation of agro-industrial residues inherent to any production process. These residues are almost always suitable for further processing and generation of by-products, thus reducing waste. Compounds with antitumor potential have been found in many agro-industrial residues, usually natural products derived from plants. The objective of this work is to bring scientific evidence about the possibilities of using agro-industrial residues as a source of compounds with antitumor potential. Therefore, a descriptive and exploratory study was carried out using bibliographic research of studies carried out between the years 2014 to 2020. The results found show that these residues have a cytotoxic, anti-metastatic, anti-proliferative, and apoptosis-inducing effect, making it possible to use them in food and drug formulations for the treatment of cancer cells.

KEYWORDS: solid waste; cytotoxic. antitumor.

POTENCIAL PARA O TRATAMENTO DO CÂNCER DE RESÍDUOS AGROINDUSTRIAIS - UMA REVISÃO

RESUMO: Com o aumento constante da urbanização global, o perfil de consumo de alimentos e o potencial para doenças crônicas como o câncer vêm mudando. O suprimento da superpopulação é papel da indústria de alimentos, que visa atender a essa demanda, aumentando, nos últimos anos, a geração de resíduos agroindustriais inerentes a qualquer processo produtivo. Esses resíduos quase sempre são adequados para posterior processamento e geração de subprodutos,

reduzindo o desperdício. Compostos com potencial antitumoral foram encontrados em muitos resíduos agroindustriais, geralmente produtos naturais derivados de plantas. O objetivo deste trabalho é trazer evidências científicas sobre as possibilidades de utilização de resíduos agroindustriais como fonte de compostos com potencial antitumoral. Para tanto, foi realizado um estudo descritivo e exploratório por meio de pesquisa bibliográfica de estudos realizados entre os anos de 2014 a 2020. Os resultados encontrados mostram que esses resíduos apresentam efeito citotóxico, antimetastático, antiproliferativo e indutor de apoptose, tornando é possível usá-los em formulações de alimentos e medicamentos para o tratamento de células cancerosas.
PALAVRAS-CHAVES: resíduos sólidos; citotóxico. Antitumor.

INTRODUCTION

Human beings are primarily responsible for the production of waste in the world, whether at an industrial, agricultural, home, or individual level, as their behavior generates waste and by-products of broad aspects, with diversified values and potentials. The increase in population directly implies greater production of waste, which generates the demand for reuse, due to the scarcity and finiteness of natural resources[26,30]. The increasing degree of industrialization of food raw materials, to meet the demand of urbanization, produces a significant increase in the generation of agro-industrial residues, which needs to be properly disposed of or reused and, in this context, the SDG - Sustainable Development Goals nº12 of Agenda 2030 "responsible consumption and production", aims to halve food waste and reduce losses along production and supply chains[32,34,37].

The UN estimates that food waste is responsible for 8 to 10% of the production of greenhouse gases, and this waste reaches 1.3 billion tons of inputs. Optimizing processes and the full use of food, through innovative technologies, can reduce this impact and curb environmental wear, allocating them to purposes that benefit human and planet health[18,29]. Several agro-industrial residues can contain bioactive compounds, which can add value to these residues and bring health benefits. Their reuse and reinsertion in human consumption impacts the reduction of environmental damage and can contribute to the reduction and control of chronic diseases, including cancer[13,22]. The occurrence of these diseases has been growing since a large part of the world population is located in urban areas, with exhausting routines, rush, stress, poor diet and sedentary lifestyle, lifestyles that increase health risks[34,43].

Bioactive compounds are antioxidant substances, classified according to their chemical structure, which plays a fundamental role in food metabolism, having a direct action on the DNA, providing color, aroma, and flavor, protecting the plant against pests and predators. In the human body, they act by creating functional interactions to prevent or treat chronic diseases, including cancer, as they have synchronous actions against carcinogenesis[42]. Cancer is a disease in which abnormal cells replicate uncontrollably and destroy tissue in the body. The word Cancer comes from the Greek karkinos, which means "crab", which is related to the disease because the increased volume of the affected tissue had the appearance of a crab's legs, which facilitates the uncontrolled proliferation and multiplication of these abnormal cells, spreading them through metastases that circulate through the bloodstream or lymphatic vessels and affect the human body in different tissues and organs. These cells replicate quickly and can generate malignant tumors called malignant neoplasms – cancer[6].

The use of natural products derived from plants and other organisms is gaining more and more space in the development of chemotherapy applied to treat various types of diseases, including cancer[37]. In this context, the objective of this work is to bring scientific evidence about the possibilities of using agro-industrial residues as a source of compounds with antitumor potential.

AGRO-INDUSTRIAL RESIDUES

Brazil recorded an income of R$ 699.95 billion in 2019, being the second largest exporter of processed foods in the world, this value is equivalent to 9.6% of the annual GDP[9]. This increase directly reflects the greater production of agro-industrial residues, since this is one of the most complex industries in terms of production and economy, due to the strong influences it suffers from climatic conditions, soil, and sociocultural factors[37].

The National Solid Waste Policy, implemented in 2010, has since proposed the prevention and reduction of waste generation, proposing the practice of sustainable consumption habits and a set of instruments to ensure increased recycling and reuse of solid waste and the environmentally appropriate disposal of these wastes[1]. According to the Brazilian Standard NBR – 10004[4], solid waste is defined as the result of community activities, of the industrial, domestic, hospital, commercial, agricultural, service, and sweeping origin. This definition also includes sludge from water treatment systems, as well as certain liquids whose particularities make their release into the public sewage system or water bodies unfeasible.

According to data from the National Supply Company[12], national grain production is estimated to reach 271.7 million tons, an increase of 14.7 million tons compared to the 2019/2020 harvest. The forecast for the planted area is that it will reach 68.6 million hectares, with emphasis on soybeans with a cultivation area of 38.6 million hectares, an increase of 4.2%, and corn with 18.4 million hectares with an increase of 8.8%. However, the post-harvest of grains faces difficulties in reducing losses, which can vary from 10 to 50% depending on the product, the region, and the technologies used[17,24].

The agro-industrial raw material processing industries that generate residues are mostly from the processing of various cultures. Most agro-industrial residues have high nutritional value (sources of proteins, carbohydrates, fibers, and bioactive compounds), and can be reused by the pharmaceutical, food, and chemical industries[23,37].

In the fruit pulp processing industry, the main residues generated are, depending on the type of processed fruit, peel, seeds or pit, and bagasse. These residues have in their composition vitamins, minerals, fibers, and antioxidant compounds that are important for physiological functions. However, in most factories, they are wasted still having a long way to go in the processing of these residues to add financial value and better use of their compounds beneficial to health[39].

Waste can present high problems when its final disposal is made, becoming a potential pollutant, in addition to representing, many times, losses of biomass and nutrients with high added value. Another problem caused by this high generation of waste originating from agricultural, commercial, and industrial activities, when placed in landfills under anaerobic conditions, results in the origin of methane, a negative consequence that favors increasing global warming[22,37].

To make the best use of these residues, it is necessary to know their composition, assess the nutritional potential and toxicity of their substances, to determine their employability that brings benefits to human and environmental health. The best use of this industrial waste collaborates with three axes of the SDGs, such as the fight against hunger, sustainability, and health[9,35].

ILLNESSES

A poor diet is defined as a diet lacking in fruit, vegetables, legumes, cereals, and grains, in addition to high consumption of saturated fats, sodium, and sugars. The passing of years has provided an increase in the world population, coupled with the significant increase in urbanization, and this has been related to the increase in diseases related to food, sedentary lifestyle and lifestyle, such as obesity, cardiovascular diseases, some types of cancers and type 2 diabetes[41,44].

These lifestyle changes enhance the emergence of cancers since among their causes is exposure to harmful agents such as disease promoters, poor diet, and genetic load. Free radicals, resulting from the natural oxidation necessary for aerobic life in energy metabolism, are related to the appearance and growth of tumors by interacting with DNA, RNA, proteins, and other oxidizable substances. Cancer has been growing rapidly and is threatening health around the world. The National Cancer Institute (INCA) estimates that, in Brazil, the incidence of cancer among men and women will be 625,000 new cases per year in 2022[25].

In the last decade, it was found that 70% of anti-tumor substances known in the world are of natural origin or derived from natural products. The chemopreventive capacity of these substances of plant origin on cancer is related to the biological mutability caused by them, such as antioxidant, anti-inflammatory, immune and hormonal system regulatory activity, cell anti-proliferative action, and induction of apoptosis[2,22,40].

It is known that eating habits can directly contribute to the emergence of malignant neoplasms, as well as helping to fight these diseases through their bioactive compounds such as polyphenolics[19]. Bioactive compounds, present in many plant residues, have antioxidant action, thus helping to fight free radicals, inhibiting the growth of harmful cells, playing a fundamental role in food metabolism, having a direct action on the DNA, providing color, aroma, and flavor, protecting the plant from pests and predators. In the human body, they act by creating functional interactions to prevent or treat chronic diseases, including cancer, as they have synchronous actions against carcinogenesis[2,40].

These compounds present in food are naturally used with the direct consumption of food but are not always used by the food industry, often these bioactive compounds remain largely in waste, such as bagasse, bark, seeds, pit and leaves. One way to reduce this loss is the full use of residues, using them in formulations or the extraction of all nutritional content for applicability in foods and drugs[22,29,37].

AGRO-INDUSTRIAL RESIDUES WITH ANTITUMOR POTENTIAL

Table 1 presents a series of studies published in recent years that demonstrate the potential of compounds present in agro-industrial residues for the prevention and combat of cancer-related health problems. Some studies analyzed residues from the food industry and reported finding antitumor potential in solid residues from the coffee industry in the extraction of coffee, the olive groves in the production of olive oil, grapes, and citrus fruits in the production of juices, foods, and beverages. These studies, although initial, make it possible to relate the use of these residues in the fight against cancer[20,36].

Industrial residues from olive groves are promising in the fight against cancer. Studies have found that phenolic compounds extracted from the olive leaf have an anticarcinogenic effect on breast, colon, stomach, and leukemia cancers. This demonstrates that the flavonoid morin and olive leaf extract have cytotoxic activity against certain malignant cell lines, significantly reducing the condition of cell proliferation, inducing apoptosis, and inhibiting the proliferation of metastases without presenting cytotoxicity to the organism[36].

The study by Pereira et al.[20] demonstrated that the flavonoid morin and olive leaf extract showed cytotoxic activity against the human lung cell line H460, decreasing cell viability in a concentration-dependent manner, with an EC50 of 220.3±1.08 μM for morin, as they induced cell death by apoptosis, altering the mitochondrial function of H460 cells. Ko et al.[28] obtained a similar result in olive extracts with antitumor activity for H460 cell lines above 70%, with morin being more effective depending on the contact time and concentration.

Bermúdez-Oria et al.[8] evaluated the antiproliferative effect of new modified pectins extracted from olives on bladder cancer with a high content of polyphenols associated with pectin-rich polysaccharides and found significant in vitro antiproliferative capacity against four human bladder cancer cell lines, RT112, T24, J82, and SCaBER, reducing the expression of galectin[-1] and galectin-3 and significantly inhibiting erythrocyte agglutination. In a previous study, Bermúdez-Oria et al.[7] produced three extracts of pectin modified by heat treatment and acid (citric or sulfuric) from the main by-product of olive oil production, called Alperujo, and evaluated their effect on the proliferation of colon carcinoma Caco-2 and lines of THP[-1] monocytic leukemia cells and both extracts inhibited proliferation at some concentrations ranging from 1 to 10 $mg.mL^{-1}$ and inhibited red blood cell agglutination by galectin-3, a lectin involved in tumor growth, metastasis and regulation of immune cells, which has been proposed to mediate the antitumor effects of modified pectins. The study also recognizes the contribution of polyphenols in 6 to 7%, in addition, the activation of caspase-3 in THP[-1] cells indicates that treatment with extracts rich in pectin triggers apoptosis resulting in tumor reduction.

Samet et al.[38] investigated the effect of Chemical olive leaf extract (COLE) for its potential differentiation-inducing effect on multipotent leukemia K562 cells and the results showed that the extract inhibits the proliferation of K562 cells and interrupts the cell cycle in G0/G1 and then in the G2/M phase over time of treatment, in addition to inducing apoptosis and differentiation of K562 cells towards the monocyte lineage, which demonstrates therapeutic effects of the olive leaf on cancer cells.

Another sector with a large generation of waste is citriculture, where approximately 50% of the orange fruit is not used in juice processing, these wastes contain biomolecules, such as phenolics and essential oils that may have antitumor potential.[15] Francisco et al.[21] observed and characterized antioxidant activities of up to 94.87% in Pêra orange residues and the influence of these compounds on the viability of cancer cells SCC9 (oral carcinoma) and found that incubation with conjugated linoleic acid reduced the proliferation of these cells in regarding control and suggests that conjugated linoleic acid may be cytotoxic to human tumor cells also in vivo, demonstrating the potential for the exploitation of residues for their biological activities as antioxidants, antitumor, and antibiotics.

In the manufacture of citrus fruit juices, the peel is seen as a residue generated on a large scale, which is rich in bioactive compounds, such as flavonoids and phenolics. Diab[16] incubated HL-60 human leukemia cells with alcoholic extracts of lemon, grapefruit and tangerine peel and verified cytotoxic activity proportional to the concentration for the three extracts, with tangerine peel extract considered moderately active, with IC50 value =77.8 mcg/mL, while the other two extracts showed low cytotoxic activity. Furthermore, the author[16] also found that the three extracts increased the viability and proliferation of mouse splenocyte cells, demonstrating the non-cytotoxicity of the extracts and their immunostimulant activity in healthy cells.

In a study by Ferreira, Silva, and Nunes[20] it was observed that the hydroalcoholic extract of tangerine peel, purified through the RP-SPE technique as a way to eliminate non-phenolic compounds, showed antiproliferative activity against the breast carcinoma lineage BT-474, with IC50 results = 167.2 $mcg.mL^{-1}$ after 24 h of incubation and 174.5 $mcg.mL^{-1}$ after 48 h of incubation. In this same study, the main flavonoids found in the extract were hesperidin (47 $mg.g^{-1}$), followed by naringin (10.43 $mg.g^{-1}$) and tangeritin (8.09 $mg.g^{-1}$) and the authors suggest the existence of a synergistic effect between hesperidin and other polyphenols as a way to explain the antiproliferative activity of the extract. Also highlighted is the potential of the combined use of hesperidin and tangeritin with conventional chemotherapeutics, such as cisplatin[3] and doxorubicin[33] due to their potentiating effects of these drugs.

Viticulture also generates large amounts of waste, most of which is bagasse (seed and bark). The production of 100 L of wine generates 20 kg of bagasse[10]. De Sales et al.[14] studying white grape pomace, found that the ethanol extract was able to reduce viable cells of human hepatocarcinoma HepG2 as a function of the extract concentration, where a decrease of 30%, 40%, and 70% was observed after incubation with 75, 150 and 300 $\mu g.mL^{-1}$ and the authors report that the extract was able to increase mitochondrial respiration, particularly the fraction of oxygen consumption used to drive ATP synthesis and these effects were accompanied by an increase in the antioxidant capacity cell phone.

Di Meo et al.[15] evaluated the antitumor activity of semi-polar extracts of grape seeds and grape skins of the Aglianico (AG) and Falanghina (FG) varietals against human mesothelioma cell lines (MSTO, NCL, and Nes2). The authors found that only the seed extracts of the FG and AG varietals reduced by 30% and 40%, respectively, the cell viability of the three strains at a concentration of 350 $mcg.mL^{-1}$, however, at the same concentration, both extracts significantly reduced colony formation and cell migration. The increase in apoptosis was significant in the MSTO strain, being 20% with FG and 35% with AG. This effect is explained by the increased expression of the BAX protein, which causes permeabilization of the mitochondrial membrane and, consequently, the release of cytochrome c, resulting in cell death. In a metabolomic analysis of the grapes, it was found high concentrations of proanthocyanidins in fruit seeds, especially in the Aglianico varietal, while these substances were practically absent in the skins, so the presence of these compounds is strongly correlated with the antiproliferative activity of seed extracts[15].

In a study by Messina et al.[32] the phenolic extract obtained from the Nero d'Avola grape skin, using from 10 $mcg.mL^{-1}$, it was verified a decrease in the cell viability of the Hep-G2 lineage of liver cancer, being the best results were obtained with extracts at a concentration of 50 $mcg.mL^{-1}$, where cells incubated for 72h suffered a reduction of more than 80% in viability. The authors also found that proanthocyanidins are the main phenolics identified in the extract, with a result of 2551 $mg.L^{-1}$, so these compounds can be important indicators of the antiproliferative activity of the grape skin residue. In a study by Martins, Macedo, and Macedo[31] with grape pomace biotransformed with tannase, the extracts obtained were able to reduce the activation of the transcription factor NF-kB p65, the production of IL-8 (interleukin 8), PGE2 (prostaglandin E2) and ROS (reactive oxygen species) in a Caco-2 cell culture showing that GPE winemaking may have a potential intestinal anti-inflammatory activity.

Coffee is a beverage consumed worldwide that contains several phytochemicals that are beneficial to health. However, coffee production generates a large amount of waste, reaching 50% of the total produced, the main ones being bark, pulp, and sludge, which concentrate significant amounts of phenolic compounds[27]. Among them, Kahweol acetate (KA) stands out, which performs an antitumor action on human tumor cells, Choi et al.[11] demonstrated evidence for the anti-metastatic effects of kahweol acetate (KA) on human fibrosarcoma cells, through reduced expression and activity of metalloproteinase-9 (MMP-9) induced by phorbol 12-myristate 13-acetate (PMA) and attributed these antitumor effects of KA to inhibition of Akt/JNK1/2/p38 MAPK phosphorylation and down-regulation of NF-κB activation, causing a decrease in MMP-9 expression, potentiating KA as a chemotherapeutic agent in the prevention of metastatic tumor. Another coffee residue is the dregs resulting from the production of espresso coffee and Balzano et al.[5] found that the ethanol extract obtained from this sludge has a promising antiproliferative activity in human lung carcinoma cells (A549), with an IC 50 value of 61.2 $\mu g.mL^{-1}$ comparable to that given by the positive control of vinblastine (value de IC 50 of 67.3 $\mu g.mL^{-1}$).

Residues	Autor (year)	Results
Olive leaf extract	Pereira et al.[19]	The olive extract affected the cell viability of the H460 lineage, inducing cell death by apoptosis.
Residue from the extraction of olive oil	Bermúdez-Oria et al.[28]	Extracts exhibited in vitro antiproliferative capacity against four human cell lines BC, RT112, T24, J82 and SCaBER
Residue from the extraction of olive oil	Bermúdez-Oria et al.[8]	Extracts inhibit in vitro cell proliferation Caco-2 and THP^{-1}.
Olive leaf extract	Samet et al.[7]	It inhibits the proliferation of K562 cells and interrupts the cell cycle in G0/G1, induces apoptosis and differentiation of K562 cells towards the monocyte lineage.
Lipases obtained from orange residue	Francisco et al.[15]	Showed cytotoxic activity to an oral cancer strain
Extracts of lemon, grapefruit and tangerine peel	Diab.[21]	Mandarin peel exhibited moderate cytotoxic activity (IC50 = 77.8 g/mL) against HL60 cells, whereas grapefruit and lemon peels were ineffective antileukemia.
Tangerine peel extract	Ferreira, Silva and Nunes[16]	Phenolic extract showed antiproliferative activity against cell lineage BT-474.

Semi-polar extracts of grape seeds and grape skins of the Aglianico (AG) and Falanghina (FG)	Di Meo et al.[3]	The seed extracts of the FG and AG varietals reduced by 30% and 40%, respectively, the cell viability of the three strains at a concentration of 350 mcg. mL^{-1}, however, at the same concentration, both extracts significantly reduced colony formation and cell migration.
White grape pomace extract	De Sales et al.[33]	The ethanol extract was able to reduce viable cells of human hepatocarcinoma HepG2 as a function of the extract concentration, where a decrease of 30%, 40%, and 70% was observed after incubation with 75, 150 and 300 $\mu g.mL^{-1}$.
Nero d'Avola grape skin extract	Messina et al.[4]	Using from 10 $mcg.mL^{-1}$, it was verified a decrease in the cell viability of the Hep-G2 lineage of liver cancer, being the best results were obtained with extracts at a concentration of 50 $mcg.mL^{-1}$, where cells incubated for 72h suffered a reduction of more than 80% in viability.
Biotransformed grape pomace	Martins, Macedo and Macedo[31]	Anti-inflammatory effects on Caco-2 cells
Kahweol acetate (KA), a coffee-specific diterpene	Choi et al.[11]	Anti-metastatic effects of kahweol acetate (KA) on human fibrosarcoma cells.
Espresso grounds extracts	Balzano et al.[5]	Significant antiproliferative activity against A549 and C32 cancer cell lines.

Table 1. Summary of the most relevant studies published in recent years on the use of agro-industrial residues with anticancer potential.

CONCLUSION

The scientific evidence raised in this review demonstrates that olivary residues have an antiproliferative and apoptosis-inducing capacity, while citrus fruits have a cytotoxic and antiproliferative effect associated with the flavonoids present in the extracts. Regarding the residues of winemaking, results were observed such as growth inhibition, antiproliferative effect, and apoptosis induction, associated with the content of proanthocyanidins in the extracts. Still, residues from the coffee industry were demonstrated to have antiproliferative and antimetastatic action through the presence of kahweol acetate.

Thus, the studies highlight the potential of these residues in relation to antioxidant and antitumor activity, making it possible to use them in formulations, foods, and drugs in the therapeutic or preventive treatment of cancer cells, which allows to improve the use of food and reduce waste generation, directly reducing the environmental impact and management costs. It is noteworthy that future studies may focus on improving the ways of using and applying these compounds and/or residues in food or pharmacological products

CONFLICT OF INTEREST

There is no confict of interest.

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