RADICAL SCAVENGING ACTIVITY, AND IN VITRO CANCER CELL CYTOTOXICITY OF CACTUS (*Opuntia ficus indica*) AND GRAPE PEEL (*Vitis species*) EXTRACTS

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Abstract. Red Prickly pear and red grape peels fruits are rich in phenols and flavonoids, which have been suggested to be responsible for their health benefits. Total phenolic compounds content (TPC), total flavonoid content (TFC), total anthocyanin content (TAC), their antioxidant and anticancer properties were examined. The TPC was 6.34 mg and 4.86 mg as Gallic /g DW, respectively. The total flavonoid content was 3.35 mg and 2.0 mg as qurectein/g DW, respectively. Total anthocyanin was found to be 2.65 mg/g dry weight in red grape peel. IC_{50} is used to express the amount or concentration of extracts needed to scavenge 50% of the free radicals. The value of IC_{50} is inversely proportional to the scavenging activity of the peel extract. The scavenging activity of the methanolic extract (100 µg/ml) of prickly pear peel (58.65%) and red grape peel (49.72%) was significantly lower than that of the synthetic antioxidant BHT (79.36%). Prickly pear and red grape peels methanolic extract exhibited cytotoxic effects on cancer human cells in a dose dependent manner assessed by MTT assay. Treatment with methanolic extract of prickly pear and red grape peels for 24 h resulted in a significant differences at $p \geq 0.05$ in cell viability for all types of Human cancer cell lines. A significant increase was observed in hepatocellular carcinoma cell line (HePG 2) 33.5% treated with prickly pear peel extract higher than that found in red grape peel 16.20%. Pronounced cytotoxic activity of red grape peel extract was observed in human colon carcinoma (HCT116) 24.50% higher than that found in prickly pear peel extract 20.6%.Low cytotoxic activity of prickly pear peel extract was observed in lung carcinoma cell line (A549) 9.86% lower than that found in red grape peel 12.03%.Low cytotoxic activity of red grape peel extract was observed on human hepatocellular carcinoma cell line (HePG 2) 16.20% lower than that found in red prickly pear peel extract 33.5%. The results suggest that red prickly pear and red grape peels fruits are rich in active constituents such as: phenols and flavonoids , which have been suggested to be responsible for their antioxidant and anticancer effects.

Keywords: Red prickly pear; red grapes; peels; phenolic; flavonoid; antioxidant; anticancer.

INTRODUCTION

The demand for natural antioxidants is increasing because of public awareness of their health benefits. Plant antioxidants have been increasingly used to substitute for synthetic antioxidants in the food, pharmaceutical and cosmetics industries [35, 57]. Some of the artificial dyes are known to be a risk to human health and natural dyes have potential health benefits [36, 51]

Prickly pear (*Opuntia ficus indica*) is a member of the *Cactacae* family. This cactus produces an edible prickly pear that is consumed as a fresh fruit. It has been reported that the outer coating of this fruit is approximated 45% to 50% of the total weight and it is managed as a waste of the agro-industrial process, which means that those by-products can be improved as a natural and economic source of natural antioxidants [3, 22, 28, 38].The nutrients and chemical composition of the prickly pear (*Opuntia ficus-indica*) fruit have been reported [39]. Aspects covered have included: contents of phenolic and flavonoids compounds [39] .

Grapes (*Vitis* species) are members of the family *Vitaceae*. Grape waste contains a large amount of phenolic compounds with antiradical activity, which is claimed to have various health benefits such as protection against atherosclerosis, coronary heart disease and cancer [18, 40].

Considerable attention has been focused on the potential beneficial effects on human health of anthocyanins and their derived compounds in grapes and their by-products. Such benefits include free radical scavenging and antioxidant activity, antimicrobial and antiviral activity, prevention of cardiovascular disease, protective effect against hepatic damage and disease, anticancer and antimutagenic activity [6, 50].

In order to approach the agro- industrial wastes as natural sources of natural pigments and antioxidants with application in food industries, the main objective of this study was to evaluate *in vitro* the potential activity of red prickly pear peel and red grape peel extracts as antioxidant and anticancer agents.

MATERIALS AND METHODS

Materials

Plant materials

Skin of red prickly pear fruits (*Opuntia ficus-indica* L.) variety El-frawla and skin of red grapes fruits (*Vitis vinifera* L.) variety Roumy Ahmer were obtained from the local market at Giza, Egypt. The red prickly pear peel and red grapes peels fruits were cut into small pieces and stored in refrigerator until extraction.

Solvents

All solvents were of analytical grade (from Sigma-Aldrich), purified and distilled.

Chemicals and Reagents

All chemicals in the present study were of high analytical grade. DPPH (**1, 1**, di phenyl-2-picryl hydrazyl radical), folin Ciocalteu phenol reagent and gallic acid (3, 4, 5-trihy-droxybenzoic), quercetin, butalated hydroxyl toluene, MTT (3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyl tetrazolium bromide), antibiotic-antimycotic mixture (Potassium

Penicillin, Streptomycin Sulfate and Amphotericin B) and L-glutamine were purchased from Sigma chemical Co., Saint Louis, USA .

Preparation of samples

The fresh samples were air dried and then dried in an oven at 40°C .The dried samples was powdered for the routine analysis of major constituents.

Preparation of plant extracts

The samples were extracted. Briefly, 10 g of the dried powder from red prickly pear and red grape peels were soaked with 100 ml of 80% methanol and shaking at room temperature for 48 h. The extracts were filtered and the extraction was repeated twice. The resulting methanolic extracts were used for the determination of total phenolic, flavonoid, antioxidant activity and cytotoxic effects on four different human cancer cell lines (A549, HCT116, MCF-7, HePG2).

Quantitative determination of anthocyanin.

Anthocyanin was determined according to [25].

Determination of total phenolic content

The colorimetric method of folin Ciocalteu reagent as described by [26] was employed for the determination of phenolic compounds.

Determination of total flavonoid content.

Total flavonoid content was determined according to [27]

Biological studies

***In vitro* determination of antioxidant activity**

Free radical scavenging assay

The free radical scavenging effect of the red prickly pear peel methanolic extracts were assessed by the decolouration of a methanolic solution of DPPH (1,1-Diphenyl -2-picryl hydrazyl) radical (violet colour) according to [7].

***In vitro* determination of anticancer study in prickly pear and red grape peels**

Four different cancer cell lines : Human Colon Carcinoma (HCT116), Lung carcinoma cell line (A549) Human Caucasian breast adenocarcinoma (MCF7) and Human hepatocellular carcinoma cell line (HePG 2) were used according to Mosmann (1983) [37].

Preparation of extracts

10 gms of dried prickly pear peel and red grape peel were separately added to 100 ml of methanol and the extracts were obtained using soxhlet apparatus for 8 hrs. The methanolic extracts were then filtered and the filtrate was concentrated by rotary evaporator at 45-50 ^{0}C. The extracts were stored in a refrigerator at 4°C for further use .

Preparation of test solution

For Cytotoxicity studies, weighed test extracts were separately dissolved in distilled DMSO and volume was made up with DMEM supplemented with 2% inactivated FBS to obtain a stock solution of 1 mg/ml concentration and sterilized by filtration. Serial two fold dilutions were prepared for carrying out cytotoxic studies.

Procedure

All the following procedures were done in a sterile area using a Laminar flow cabinet bio safety class II level (Baker, SG403INT, and Sanford, ME, USA). Cells were suspended in RPMI 1640 medium for the four cell lines. The media are supplemented with 1% antibiotic-antimycotic mixture (10,000U/ml Potassium Penicillin, 10,000µg/ml Streptomycin Sulfate and 25µg/ml Amphotericin B), 1% L-glutamine and 10% fetal bovine serum and kept at 37 °C under 5% CO_2. Cells were batch cultured for 10 days, then seeded at concentration of 10x103 cells/well in fresh complete growth medium in 96-well microtiter plastic plates 37 °C for 24 h under 5% CO_2 using a water jacketed Carbon dioxide incubator (Sheldon, TC2323, Cornelius, OR, USA). Media was aspirated, fresh medium (without serum) was added and cells were incubated either alone (negative control) or with different concentrations of sample to give a final concentration of (100 – 50 – 25–12.5–6.25–3.125–0.78 and 1.56 µg/ml). After 48 h of incubation, medium was aspirated, 40µl MTT salt (2.5µg/ml) were added to each well and incubated for further four hours at 37°C under 5% CO_2. To stop the reaction and dissolving the formed crystals, 200µl of 10% Sodium dodecyl sulphate (SDS) in deionised water was added to each well and incubated overnight at 37ºC. A positive control which composed of 100µg/ml was used as a known cytotoxic natural agent who gives 100% lethality under the same conditions . The absorbance was then measured using a micro plate multi-well reader (Bio-Rad Laboratories Inc., model 3350, Hercules, California, USA) at 595nm and a reference wavelength of 620nm. A statistical significance was tested between samples and negative control (cells with vehicle) using independent t-test by SPSS 11 program. DMSO is the vehicle used for dissolution of plant extracts and its final concentration on the cells was less than 0.2%.

The percentage growth inhibition was calculated using following formula:

% cell inhibition = 100- {(AT- Ab) /(Ac – Ab)} x 100

where,

AT= Absorbance value of extract

Ab= Absorbance value of blank

Ac= Absorbance value of control

Statistical Analysis

Data were statistically analysed using Costat statistical package data according to [49].

RESULTS

Total phenolic content, total flavonoid content and total anthocyanin content of prickly pear and red grape peels

Data presented in Table (1) show the total phenolic and total flavonoid of methanolic extract of red prickly pear and red grape peels.

As can see in Table 1, the total phenolic content was 6.34 mg as gallic /g DW for red prickly pear and

Table 1. Total phenolic (TP) and total flavonoid (TF) in 80% methanolic extract of red prickly pear peel and total anthocyanin(TA) in red grape peel

Plant extract	Total phenolic (TPC) mg as gallic acid /gDW	Total flavonoid (TFC) mg as qurestin /gDW	Total anthocyanin (TAC) as delphenidin 3,5 sumboside/gDW
Red Prickly pear peel	6.34 ± 0.02	3.35 ± 0.10	--
Red grape peel	4.86 ± 0.011	2.0 ± 0.058	2.65+ 0.054

All values are the mean of three replicate ± Standard deviation

Table 2. Percent of DPPH inhibition of prickly pear and red grape peels methanolic extracts

Concentrations / Plant extract	Antioxidant inhibition %		
	25µg/ml	**50µg/ml**	**100 µg/ml**
Prickly pear peel	15.65±0.32	27.85±0.69	58.65±0.72
Red grape peel	11.08±0.27	23.31±0.76	49.72±0.56
BHT	29.47±0.76	57.21±0.34	79.36±0.34

All values are the mean of three replicates± SD

4.86 mg as gallic/g DW for red grape peel.The results show that (TPC) was highest in red prickly pear peel (6.34 mg as gallic/g DW) compared to (TPC) in red grape peel (3.35mg as gallic/g DW). The total flavonoid content of the peels of both plants was highest in prickly pear peel (3.35 mg as qurestin/gDw) followed by red grape peel (2.0 mg qurestin/gDW). The total anthocyanin content (TAC) in red grape peel methanolic extract as assessed by Spectrophotometer was 2.65 mg as delphenidin 3,5 sumboside /g based on dry weight.

Antioxidant activity of red prickly pear and red grape peels methanolic extracts

The antioxidant activity of prickly pear and red grape peels methanolic extract at different concentrations (25µg/ml, 50µg/ml and 100µg/ml) were evaluated as free radical DPPH scavenging activity. Data presented in Table 2 and Figure1 show the mean values of radical DPPH scavenging activity expressed as IC50 (concentration µg/ml for 50% inhibition) of prickly pear peel, red grape peel extracts and butylated hydroxyl toluene (BHT) as synthetic antioxidant agent.

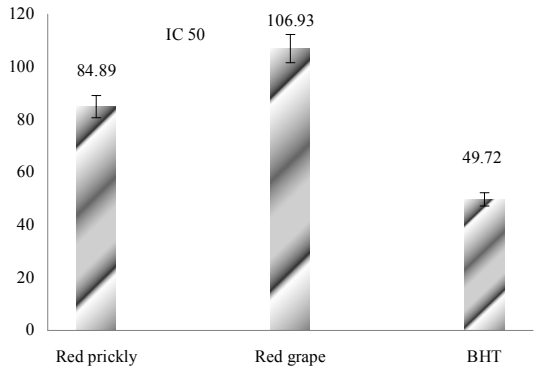

Figure 1. Concentrations of prickly pear and red grape peels extracts necessary for 50% antioxidant inhibition (IC50)

The value of IC_{50} is inversely proportional to the scavenging activity of the peels extract. The scavenging activity of the methanolic extract (100 µg/ml) of prickly pear peel (58.65%) and red grape peel (49.72%) was significantly lower than that of the synthetic antioxidant BHT (79.36%).

It is clear that the free radical scavenging activity of red prickly pear peel was significantly higher than of red grape peel .This difference between red prickly pear peel and red grape peel may be due to that red prickly pear peal contain higher amount of total phenolic and total flavonoid (6.34 mg, 3.35mg, respectively) than that of red grape peel (4.86mg, 2mg, respectively).

***In vitro* Cytotoxicity studies**

It is known that different cell lines might exhibit different sensitivities towards an antiproliferative compound, so the use of more than one cell line is therefore considered necessary in the detection of antiproliferative compounds.

The effects of methanolic extract of prickly pear and red grape peels on Human Colon Carcinoma (HCT116), Lung carcinoma cell line(A549), Human Caucasian breast adenocarcinoma MCF7)and Human hepatocellular carcinoma cell line (HePG 2)are presented in Table 3.

Prickly pear and red grape peels methanolic extract exhibited cytotoxic effects on cancer human cells in a dose dependent manner assessed by MTT assay. Cells treated with 100 µg /ml of prickly pear and red grape peels extract for 24 h resulted in a significant differences at $p \geq 0.05$ in cell viability for all types of Human cancer cell lines. Remarkable differences between the responses of human cancer cells lines for treatment with prickly pear and red grape peels extracts were found. A significant increase was observed in hepatocellular carcinoma cell line (HePG 2) was 33.5% treated with prickly pear peel extract higher than that those found in red grape peel extract 16.20%.

On the other hand, pronounced cytotoxic activity of red grape peel extract was observed in human colon carcinoma (HCT116) 24.50% higher than that those found in prickly pear peel extract 20.6%.

Low cytotoxic activity of prickly pear peel extract was observed in lung carcinoma cell line (A549) 9.86% lower than that those found in red grape peel 12.03%.

Whereas, the prickly pear peel extract did not affect the viability of lung carcinoma cell line (A549) 9.86%.

Table 3. Cytotoxic activity (% Inhibition) of prickly pear peel and red grape peel methanolic extract at concentration (100 µg/ml)

Cancer type / Plant extract	Human Colon Carcinoma (HCT116)	Lung carcinoma cell line (A549)	Human Caucasian breast adenocarcinoma (MCF7)	Human hepatocellular carcinoma cell line (HePG 2)
Prickly pear peel	20.6 ± 0.25	9.86 ± 0.50	20.5 ± 0.25	33.5 ± 0.30
Red grape peel	24.50 ± 0.20	12.03 ± 0.25	18.70 ± 0.20	16.20 ± 0.17

All values are the mean of three replicates ±standard deviation

Data presented in Table (3) show that among the four cancer cells tested, prickly pear peel extract markedly decreased the viability of both cell lines hepatocellular carcinoma cell line (HePG 2) and colon carcinoma (HCT116) 33.5 % and 24.5% respectively in a dose-dependent (100µg/ml).

DISCUSSION

It has been found that the total phenolic compounds content in prickly pear peel was three fold higher than previously reported by [19] in red skinned cactus pear *Opuntia ficus indica, Opuntia stricta* and *Opuntia undulate* (2.188, 2.04 and 1.64 mg/g DW) respectively, [14] (1.33 mg gallic acid /gDW) in *Oputia dillenii* Haw fruit (ODHF) and [11] (0.44 mg to 3.76 mg gallic acid /gDW). On the other hand, [41] found that the total phenolic compounds of xoconostle (*Opuntia matudae*) content was 19.9 mg and 17.03 mg as gallic acid /g DW in pericarb and mesocarb, respectively which was higher than our results.

The total phenolic content in red grape peel was higher than that previously reported by [2, 30] (3.51 mg, 0.64mg, 1.19 mg and 0.90 mg as gallic acid/g based on D.W) in the skin of grape varieties Mandilaria, Voidomatis, Asyrtiko and Aidani respectively and [46] (1.43 mg to 2.46 mg as gallic acid / g), [48] (1.93 mg and 1.83 mg as gallic acid/g) in Isabel grapes and Niagara grapes peel, respectively. On the other hand our results are lower than those found by [12] (5.60 mg and 7.33 mg as gallic acid / g based on dry weight) in the skin of grape by using non-conventional techniques and two solvents system methanol and ethanol respectively and [56] (14.99 mg and 20.33 mg as gallic acid /g dry weight) in skin of grape *Vitis vinifera* L. (Merlot and Chardonnay), respectively and [10] (790 mg as gallic acid /g dry weight) in skin of grape extracts, [34] (90 mg to 126 mg as gallic acid /g) in grape skin of winemaking residues, [43] (13.8mg as gallic acid /g fresh weight) in skin of wild grapes Shiohitashibudou, [9] (750 mg as gallic acid /g dry weight) in skin of red grape (*Vitis vinifera* L.), [16] (21.4–26.7 mg as gallic acid /g dry matter)in red wine grape pomace, [45] (6.6 to 18.39 mg as catechin /g dry weight) .It has been found by [32, 44] that the average of total phenolic content was 0.875mg and 1.851mg as gallic acid / g based on fresh weight in grape skin extracts of 14 *Vitis vinifera L.* (seven white cultivars and seven red cultivars respectively). Ivanova *et al*. (2011) [29] mentioned that total phenolic content (48.3mg and 33.3 mg as gallic acid /g fresh weight) in red grape skin varieties such as Vranec and Merlot, respectively. Aguirre *et al*. (2010) [1] found that total phenolic content was 1.4 mg as gallic acid/ g fresh weight in the skin of grapes *(Vitis vinifera* L.).

The differences in phenolic content could be related to the part of fruit used for making the extract. In this work *O. ficus-indica* samples were processed with the peel whereas the other authors used the fruit pulp only. Phenolics might tend to accumulate in the dermal tissues of plant body due to their potential role in protection against UV radiations, acting as attractants in fruit dispersal, and as defence chemicals against pathogens and predators [54].

Data presented in Table 2 show that there are significant differences in the total flavonoid content**.**The total flavonoids of the methanolic extract of prickly pear peel was 3.35 mg as quercetin /g DW higher than found in red grape peel extract 2.00 mg as quercetin /g DW).

It has been found that the total flavonoid content in prickly pear peel more than that obtained by [11] (0.076 to 0.66 mg rutin / g DW). Fernandez Lopez *et al*. (2010) [19] found that the total flavonoid in the extracts of three species of Spanish red-skinned cactus pear fruits (*Opuntia ficus indica, Opuntia undulata* and *Opuntia stricta*) was 51.1 µg , 161.1 µg and 51.1 µg/g fresh weight, respectively . Chang *et al*. (2007) [14] found that the flavonoid content of the peel in *Opuntia dillenii* Haw fruit (ODHF) was 0.035 mg/g fresh sample. Kuti (2004) [33] found that total flavonoid (g fresh wt.) in four cactus (*Opuntia species*) *Opuntia ficus indica* (geeen skinned), *Opuntia lindheimeri* (purple skinned), *Opuntia streptacantha* (red skinned) and *Opuntia stricta var.stricta* (yellow skinned) was 69.5 µg, 93.5 µg, 54.8 µg and 9.8 µg, respectively.

Osorio- Esquivel *et al*. (2011) [41] found that the total flavonoid in the pericarp of acidified acetone extract and acidified methanol extract in *Opuntia Joconostle cactus* was 0.68mg (+)-catechin equivalents (CE) / g based on fresh weight and 0.46 (+)-catechin equivalents (CE) / g based on fresh weight, respectively.

Red grape peel is a source of nutritional anti-oxidants, such as polyphenols, flavonoids as well as biologically active dietary components. The total flavonoid content in red grape peel more than that obtained by [9] (1.47mg as CE /g dry weight). On the other hand, our results are lower than those found by [12] (3.25 mg and 4.85 mg as CE/g DW) and [13] (15.1 mg as CE/ g dried skin). Poudel *et al*. (2008) [43] found that total flavonoid was (0.3 mg to 3.4 mg as QE /g fresh weight) in skin of five wild grapes and two hybrids native to Japan. Katalinic *et al*. (2010) [32] stated total flavonoid content was (0.686 mg and

1.332mg as quercetin acid /g fresh weight) in grape skin extracts of 14 *Vitis vinifera* L. (seven white cultivars and seven red cultivars respectively). Ivanova *et al*. (2011) [29] mentioned that total flavonoid content was (10.2mg, 8.80mg, 10.8mg and 3.12 mg as CE/g fresh weight) in skin of grape varieties Vranec, Merlot, Smederevka and Chardonnay, respectively. The total anthocyanin content in methanolic extract of red grape peel was 2.65 mg as delphenidin 3, 5 sumboside /g based on dry weight. It has been found the total anthocyanin content was lower than that previously reported by [34] (11mg to 17mg M_3GE (as malvidin -3-O- glucoside) /g based on dry weight) in grape skin, [45] (16.84 mg, 8.27 mg, 29.17 mg and 4.96 mg as M_3GE /g DW) in grape pomace varieties Cabernet sauvignon, Merlot, Bordeaux and Isabel respectively, Poudel *et al*. (2008) [43] found that total anthocyanin in skin of five wild grapes and two hybrids native to Japan was ranged from 0.9 mg to5 mg as M_3GE /g FW. Aguirre *et al*. (2010) [1] mentioned that total anthocyanin in skin of *Vitis vinifera* L. grapes was 80.21 mg malvidin -3-O- glucoside /100g fresh weight basis. Katalinic *et al*. (2010) [32] found that the average of total anthocyanin in skin of seven red *Vitis vinifera* L. varieties was 763mg malvidin -3-o-glucoside /Kg fresh weight. Ivanova *et al*. (2011) [29] found that total anthocyanin in skin of red grape varieties Vranec and Merlot was 8.40 mg and 7.21 mg as malvidin -3-O- glucoside /g fresh weight, respectively. The antioxidant activity may be attributed to their free radical scavenging ability due to the presence of polyphenols, flavonoids and pigments (anthocyanin) [23, 39].

Polyphenols and flavonoids have antiradical activity, which is claimed to have various health benefits such as protection against atherosclerosis, coronary heart disease and cancer [20, 39, 42, 56] .

Prickly pear peel (*Opuntia ficus-indica*) fruit extracts showed the highest protective effects of all models of lipids oxidation due to its high content of betalains, which contributes to the antioxidant activity of prickly pear fruit, [31] also specified betalain as a new class of dietary cationized antioxidant. The nutraceutical benefits of prickly pear peel are believed to their antioxidant properties related to ascorbic acid, phenolics and a mixture of betaxanthin and betacyanin pigments [41, 52].

The high concentration in the outer layers may be due to the action of light and other environmental factors that can induce flavonoid synthesis in the plant. Typically, flavonoids are found mainly in fruit skin [47]. The main functions of flavonoids in plants are pigmentation, protection of the plant from UV light and microorganisms, or regulation of enzyme activity [55].

The scavenging activity of the methanolic extract (100 µg/ml) of red prickly pear peel was found to be 58.65%.These results are agreement with [8, 11, 53] who found that the extract of prickly pear peel is very effective as an antioxidant and its health protective potential due to its capability of directly reacting and quenching DPPH radicals because of the peel contained high amounts of betanin, isobetanin and ascorbic acid. Our results are supported by [33] who found that the antioxidant activity of the extract was stronger in the purple skinned than other varieties (green skinned, red skinned and yellow skinned) due to presence of phenolic acids and flavonoids, betanin and isobetanin, which play an important role in antioxidant activity . Guzman- Maldonado *et al*. (2010) [22] who found that the antioxidant capacity of *xoconostle cv. Cuaresmeno* peel was 2.1-fold and 6.3-fold higher than that of the skin and the pulp, respectively. On the other hand [11] showed that the fruits with light-green or yellow-brown peel have higher antiradical activity and Trolox equivalent antioxidant capacity (TEAC) values compared with those with red-purple peel.

The scavenging activity of the methanolic extract (100 µg/ml) of red grape peel was found to be 49.72%. This result is higher than that previously reported by [9] (18.35%) in methanolic extract of grape skin. The total anthocyanin content was lower than previously reported by [34] (11 mg to 17 mg).

The concentration necessary for 50% inhibition of DPPH (IC_{50}) of red grape peel methanolic extract was106.93 µg lower than previously reported by [46] 316.41µg, 334.74µg, 234.53µg and 226.15 µg/ml) in methanolic extracts of four grape peel varieties Brazil (*Vitis vinifera L.*), Benitaka (*V. vinifera L.*), Isabel (*Vitis labrusca L.*) and Niagara (*V. labrusca L.*, respectively). The DPPH as IC_{50} (µg/ml extract) was lower than previously reported by [2] 55.7µg, 177.5µg, 117.0µg and 274.2µg/ml in grape skin varieties Mandilaria, Voidomatis , Asyrtiko and Aidani extracts, respectively. On the other hand, the antioxidant properties was higher than those obtained by [32] (156, 209, 239, 153, 58.0, 64.2and 158 mg GAE/l) in grape skin extracts of 14 *Vitis vinifera* red and white varieties (Vranac, Trnjak, Rudezusa , Merlot , Babic, Lasin and Plavina respectively). as DPPH radical-scavenging ability (IC_{50}), they found the IC_{50} (mg GAE/l) of red varieties grape skin extracts was in seven red grape peel varieties The high antioxidant capacity of all extracts red grape peel varieties has been observed and related to the relative amounts of polyphenolic compounds with good antioxidant properties [42].

Casazza *et al*. (2010) [12] found the antiradical power from grape skins using high pressure and temperature extraction values between 8.45 and 52.17 µg DPPH/ µl extract.

The differences in antioxidant activity may be attributed to the assay used or the solvent system and the genotypic variation.

Cancer is a global health problem with high morbidity and mortality and poses both economic and psychological challenges [17, 37] .

Red prickly pear peels was found to possess very potent inhibitory activities against all tested cell lines. These properties are in agreement with [15] who tested the effect of Juices of nine prickly pears (*Opuntia* spp.) in terms of phenolics, flavonoids, betalains and antioxidant activity *in vitro* against four cancer cell lines. Among the cancer lines tested, viability of

prostate and colon cells were the most affected with *Moradillo* cultivar because of contained the highest content of flavonoids which diminished both prostate and colon cancer cell viability without affecting mammary or hepatic cancer cells. On the other hand, *Rastrero* cultivar reduced the growth of the four cancer cell lines without affecting normal fibroblast viability, these may be attributed to the inter varietal differences among prickly pears in terms of juice properties and phytochemicals that could prevent oxidative stress and cancer.

Prickly pear peels contain several active compounds which act as phytonutrients work at a much deeper level and actually signal genes to increase production of enzymes involved in the detoxification [26].

The anti-carcinogenic actions of prickly pear peel are attributed to their content of ascorbic acid, phenolics and a mixture of betaxanthin and betacyanin pigments [52].

Red grape peel methanolic extract exhibited a pronounced cytotoxic effect for A549, HCT116, MCF-7 and HePG2 respectively cell survival at 100 µg mL^{-1}respectively as compared to that of red prickly pear . The Red grape peel is a rich source of polyphenols and resveratrol (3, 4′, 5-trihydroxy-trans-stilbene) which has anticancer properties [4, 45]. The anticancer effects of red grape peel may be attributed to the presence of resveratrol (3, 4′, 5-trihydroxy-trans-stilbene) which had the ability to modulate expression/activity of antioxidative and phase 2 drug metabolizing enzymes and scavenging free radicals [26].

Ghasemzadeh *et al*. (2012) [24] showed that resveratrol (3, 4′, 5-trihydroxy-trans-stilbene) and phenolic compounds in red grape peel are responsible for the chemo preventive properties of red grape peels. It has been found by [26] that Resveratrol acts as a natural inhibitor of cell proliferation and has been shown to possess a fascinating spectrum of pharmacologic properties. Resveratrol affects all three discrete stages of carcinogenesis (initiation, promotion, and progression) by modulating signal transduction pathways that control cell division and growth, apoptosis, inflammation, angiogenesis, and metastasis. The anticancer property of resveratrol has been supported by its ability to inhibit proliferation of a wide variety of human tumour cells *in vitro* [5].

Our results are in agreement with [3] who mentioned that methanolic grape peel extract could inhibit cancer cell growth or enhance the molecular mechanism of the chemo preventive effects on cancer.

It is evident that the antioxidants polyphenols present in the fruits are responsible for the inhibition of cancer cell growth [13, 21].

On the basis of the results obtained, prickly pear and red grape peels may play a potential role as a source of health-promoting compounds (phenolics, flavonoids) associated with antioxidant activity. Therefore, there is great promise for the utilization of prickly pear and grape peels for creating new beneficial health products for nutraceutical markets in the future.Further studies are needed to isolate the most bioactive anticancer compounds and if *in vitro* results correlate with animal experiments**.**

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