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Letter to the editor:

APPLE AS A SOURCE OF DIETARY PHYTONUTRIENTS: AN UPDATE ON THE POTENTIAL HEALTH BENEFITS OF APPLE

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Dear Editor,

Since several studies have demonstrated the pharmacological activities (anti-oxidant, anti-microbial, anti-inflammatory, anti-diabetic, anti-cancer, etc.) of fruits and vegetables, it has been suggested that a daily intake of apples is associated with the prevention of several chronic diseases, including chronic obstructive pulmonary disease, asthma and different types of cancers (Boeing et al., 2012; Kalinowska et al., 2014).

Apples, the world's second most consumed fruit after bananas, contain several nutrients together with non-nutrients such as dietary fiber, minerals and vitamins. In addition, apples possess rich contents of polyphenols, which are divided into several groups including hydroxybenzoic acids, hydroxycinnamic acids and their derivatives, flavonols, dihydrochalcones, anthocyanids, monomeric flavanols and oligomeric flavanols (Kalinowska et al., 2014). Due to the high nutraceutical values and various polyphenols of apples, apples have exhibited beneficial effects on the health against cancer, asthma and pulmonary dysfunction, cardiovascular diseases, Alzheimer's disease, decline of normal aging, weight management and diabetes (Hyson, 2011). These findings have supported the age-old saying "an apple a day keeps the doctor away".

The present report summarizes key recent studies that have demonstrated the biological and pharmacological properties of apple and its products (Table 1). We hope that this report will further spur the research on the potential application of apple, its products and its biologically active compounds for preventing several chronic diseases in humans.

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Conflict of interest

The authors declare no conflict of interest.

Table 1: Recent studies on biological and pharmacological activities of apple and its products

Effect	Summary	Reference
Anti-cancer	Pectic-oligosaccharides from apples induced caspase-dependent apoptosis and cell cycle arrest (sub-G1 arrest) in MDA-MB-231 cells, a model of human breast cancer.	Delphi et al., 2015
	Apple seed oil obtained from apple pomace contained the high percentage of unsaturated fatty acid (about 90 % of oil; Oleic acid, 46.50 %; linoleic acid, 43.81 %) and exhibited efficacy against the proliferation of CHOK1 (Chinese hamster), A549 (human lung carcinoma) and SiHa (human cervical cancer cell) cells.	Walia et al., 2014
	Pelingo apple (autochthonous red apple cultivar) strongly inhibited the proliferation of breast cancer cells, and induced cell accumulation in the G2/M phase of the cell cycle and autophagy, overexpression of p21 and inhibition of ERK1/2 activity. In addition, the Pelingo apple suppressed 12-o-tetra-decanoyl-phorbol-13-acetate (TPA)-induced tumorigenesis of JB6 P+ cells through inhibition of ERK1/2 activity.	Schiavano et al., 2015
	Apple polyphenol, which contained 65.7 % procyanidins (13 % dimers, 12.3 % trimers, 8.7 % tetramers, 5.9 % pentamers, 4.9 % hexamers and 20.9 % other polymers), 12.5 % flavan-3-ols (2 % catechin and 10.5 % epicatechin), 6.5 % other flavonoids and 10.8 % nonflavonoids, significantly suppressed migration, invasion, colony formation and adhesion of DLD-1 (human colon cancer cell line) cells. In addition, AP significantly inhibited motility of DLD-1 cells via disruption of Snail-FAK promoter interaction and inhibition of FAK downstream signaling cascades, and consequently diminished tumorigenesis and metastasis of DLD-1 cells.	Hung et al., 2015
	Apple oligogalactan potentiated the growth inhibitory effect of celecoxib in two human colon cancer cell lines (Caco-2 and HT-29 cell lines) and a CACC mouse model through influencing the expression and function of COX-2 and phosphorylation of MAPKs.	Li et al., 2014
	Apple polyphenol has cytotoxicity effect in human urinary bladder cancer cells (TSGH-8301) associated with apoptosis, G2/M arrest, and mitotic catastrophe via an alteration in mitochondrial function and ROS generation.	Kao et al., 2015
	A novel triterpenoid, named 3β-trans-cinnamoyloxy-2α-hydroxy-urs-12-en-28-oic acid (CHUA), from apple peels showed potent in vitro antitumor activity against human breast cancer (MDA-MB-231 cell). CHUA induced apoptosis in MDA-MB-231 cells via mitochondrial pathways and caspase-independent pathways.	Qiao et al., 2015
	A hospital-based case-control study suggested that the risk of colorectal cancer decreased with higher level of apple consumption, indicating the beneficial effect of apple on the risk of colorectal cancer.	Jedrychowski et al., 2010
	In a case control study in Hawaii, it has been suggested that apple (odds ratio = 0.6, 95 % confidence intervals: 0.4-1.0) and onion (odds ratio = 0.5, 95 % confidence intervals: 0.3-0.9) intake was associated with a reduced risk of lung cancer in both males and females.	Le Marchand et al., 2000

Effect	Summary	Reference
Anti-obesity and anti-diabetic effects	Apple-derived pectin modulated gut microbiota, and alleviated HFD (high-fat diet)-induced body weight gain, fat mass development, dyslipidemia, hyperglycemia, hyperinsulinism, metabolic endotoxemia and systemic inflammation in obese rats.	Jiang et al., 2016
	Young apple (30 days after blossoming) polyphenols inhibited the starch digestion by α-amylase.	Sun et al., 2016
	Methylglyoxal is a major precursor of advanced glycation end products linked to diabetes and its related complications. Phloretin from apples prevented methylglyoxal-induced cytotoxicity in human retinal epithelial cells via activation of the Nrf2 related defense pathway, indicating the potential role of phloretin as useful pharmaconutrient agent for complementary treatment/management of diabetes-related complications.	Sampath et al., 2016
	Based on meta-analysis, it has been suggested that total apple product consumption, whole apples, apple sauce and apple juice were associated with higher diet qualities than those seen in non-consumers of the same food groups. In addition, total apple consumption and whole apple consumption were associated with a lower prevalence of obesity and a lower likelihood of obesity.	O'Neil et al., 2015
	The metabolic disorders caused by high fat diet were thwarted by taking apple cider vinegar, which proves to have a satiating effect, antihyperlipidemic and hypoglycemic effects, and seems prevent the atherogenic risk.	Bouderbala et al., 2016
	The cloudy apple juice and apple peel extract of Egyptian Anna apple exhibited antihyperglycemic effects by reduction of the inflammatory response, mitigation of the oxidative stress, and normalization of the deranged lipid profile, suggesting that they might be useful therapeutic agents for treatment of deleterious complications of diabetes mellitus.	Fathy and Drees, 2016
	The effect of apple on fasting blood sugar and plasma lipid levels in Type II diabetics' patients (42-70 years old) was investigated, and found that one medium size apple in diet of Type II diabetics reduces the fasting blood sugar and plasma lipid levels.	Dange and Deshpande, 2013
	According to Finnish study involving 10,000 adults, a reduced risk of Type II diabetes was associated with apple consumption.	Knekt et al., 2002
Anti-inflammation	Dried apple peel powder increases joint function and range of motion via the inhibition of COX-2 and lipoxygenase enzymes and reduction of ROS formation.	Jensen et al., 2014
	Dietary flavonoids from modified apple reduced the inflammation-related gene expression (interleukin-11, chemokine receptor 2, chemokine receptor 10, and interleukin-2 receptor, b chain) in jejunum tissue of mice.	Espley et al., 2014
	Apple polyphenols reduce inflammation response of the kidneys in unilateral ureteral obstruction rats via decreasing the expression and activity of COX-2, downregulating the transcription factor NK-κB and up-regulating the expression of Nrf2.	Lee et al., 2014

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Effect	Summary	Reference
Hepato-protective	Apple polyphenol extract significantly enhanced the activities of superoxide dismutase and catalase and the rate of ATP synthesis and hydrolysis in the aluminum (Al)-treated rats, suggesting that apple polyphenol extract plays a role in reducing the toxic effects of Al in the liver of rats.	Cheng et al., 2014
	Cloudy apple juice significantly reduced the levels of hepatic ALT and SDH, and increased the pentoxyresorufin-O-depentylase (CYP2B biomarker) and NAD(P)H:quinone oxidoreductase-1 activities in hepatocarcinogenic N-nitrosodiethylamine (NDEA)-treated rats. These indicate that metabolic alterations induced by cloudy apple juice may protect against liver damage.	Krajka-Kuźniak et al., 2015
Antigenotoxicity	The treatment of apple juice resulted in decreasing the frequency micronucleated cells (erythrocytes and hepatocytes) in the cadmium-exposed rats. In addition, apple juice reduced the 8OHdG (8-hydroxylated guanine) levels and genetic damage in liver and peripheral blood cells.	Gomes de Moura et al., 2015
Reduction of cardiotoxicity	Polyphenol-rich apple peel extract attenuates arsenic trioxide induced cardiotoxicity in H9c2 cells via alteration of the activity of lactate dehydrogenase, superoxide dismutase, catalase, glutathione, glutathione peroxidase, thioredoxin reductase, xanthine oxidase, calcium overload and caspase 3.	Vineetha et al., 2014
Etc.	Higher apple intake was associated with lower risk of all-cause and cancer mortality in a cohort of women aged over 70 years, suggesting that an apple a day protects against death in elderly women, though reductions in the risk of cancer.	Hodgson et al., 2016

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