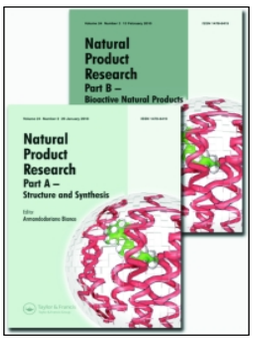

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Chemical profile and antihyperlipidemic effect of *Portulaca oleracea* L. seeds in streptozotocin-induced diabetic rats

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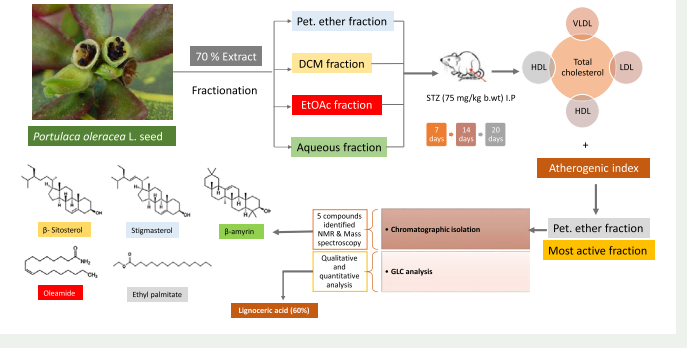
ABSTRACT

Hypolipidemic effect of *Portulaca oleracea* L. seed extract and its fractions have been studied on streptozotocin (STZ) at dose 75 mg/kg b.wt. After fractionation of the alcoholic extract; petroleum ether fraction was the most active fraction that decreased different hyperlipidemia biochemical parameters. After chromatographic analysis; oleamide, ethylpalmitate, β-amyrin, stigmasterol and β-sitosterol were identified. The GLC analysis of unsaponifiable matter revealed the presence of; lignoceric acid as a major constituent in the most bioactive fraction. In conclusion, petroleum ether fraction possessed a hypolipidemic effect in STZ-induced diabetic rats, which may be attributed to its phytosterols, fatty acid and amide compounds. The finding of the present investigation strongly demonstrates the potential of non-polar fraction of *P. oleracea* L. seed in combating hyperlipidemia in diabetic condition. So the petroleum ether fractions and its constituents can be used as hypolipdemic supplement in the developing countries towards the development of new therapeutic agents.



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1. Introduction

Portulaca oleracea L. a member of Family Portulacacea (commonly called purslane) is a herbaceous weed widely distributed throughout the world. It is a succulent, prostrate annual herb considered to possess antiscorbutic, aperients and diuretic properties. The seeds are demulcent, carminative, diuretic and slightly astringent (Uddin et al. 2014). It has an extensive old world distribution, extending from North Africa through Middle East and the Indian subcontinent to Malaysia and Australia (Sultana & Rahman 2013). The alcoholic seed extract showed antioxidant activity (Jalali et al. 2015) and Al-Sheddi et al. 2016 approved that it can ameliorate hydrogen peroxide that induced cell death in human liver cells. Additionally, Gai et al. 2016 revealed that purslane seed oil can be used as a substitute for synthetic antioxidants in food preservation and as a cosmetic ingredient. The alcoholic seed extracts showed cytotoxicity on human hepatocellular carcinoma cells (HepG2) (Farshori et al. 2014) and pain reducing effects (Farhadpour et al. 2014). The seed oil also exerted cytotoxic effects on HepG2 and human lung cancer (A-549) cell lines (Al-Sheddi et al. 2015). Furthermore, *P. oleracea* seeds had positive clinical effects on serum lipids profile in case of dyslipidemia in obese adolescents (Sabzghabaee et al. 2014, Zakizadeh et al. 2015). Dehghan et al. 2016; clinical observation showed that seed consumption alongside exercising could improve atherosclerosis plaque biomarkers in women with type 2 diabetes. The plant is also consumed as a vegetable and has been reported to be rich in different chemical constituents such as; alkaloids (Xiang et al. 2005; Li et al. 2017; Xu et al. 2017), flavonoids, coumarins, polysaccharides, omega fatty acids, terpenoids, sterols, proteins, vitamins and minerals (Zhou et al. 2015). The seed and its extract demonstrated a notable hypolipidaemic effect on human metabolism without rationalisation. There is also no data on the chemical composition of the seed responsible for this activity, which is the aim of this study. Furthermore, the literature about the chemical constituents were scanty. So, it deemed interesting to assign the fraction and compounds that may attribute to the hypolipidemic effect.

2. Results and discussion

2.1. Serum triglycerides and Serum total cholesterol

The methylene chloride fraction (DCM) and petroleum ether fraction were the most active fractions which showed a significant effect in decreasing higher level of serum triglycerides. Where the DCM fraction has rapid onset of effect, but with short duration of action, in opposite to petroleum ether fraction. After 20-days of treatment, fractions arranged according to percentage of change in their effect as follows, (Petroleum ether-F > EtOAC-F > aqueous > total extract > DCM-F) (68 > 53 > 50 > 32 > 26%). Regarding to serum cholesterol, the chloroform, petroleum ether and total extract demonstrated a significant activity. Petroleum ether fraction was the most active fraction as a percentage of change in cholesterol level was prolonged in a long time (56, 58 and 78%). While, the chloroform fraction has fluctuated in their activity (73 > 45 > 85%) (Table S1).

2.2. Serum high density lipoprotein (HDL) and Atherogenic index

The Level of HDL is decreased after injection of STZ as it is considered as a protective factor against heart diseases its level decrease in case of diabetes; total and ethyl acetate have

rapid onset of action as both give significant effect after 7-days of treatment, while other fractions started their activity after 14-days of treatment. So the ethyl acetate fraction showed the best activity as it has a longer duration of action and rapid onset and it also considered as the most active fraction for the atherogenic index.

2.3. Serum low and very low density lipoprotein (LDL & VLDL)

The result showed that the activity of fraction arranged as follows (DCM-F > total extract > EtOAC-F > aqueous-F > petroleum ether-F) as (51 > 86, 75, 33% of change) during the period of treatment, respectively. So DCM fraction is the most active fraction for lowering the level of LDL. On the other hand; fractions activity for VLDL were classified according to their effect into (petroleum ether-F > EtOAC-F > aqueous-F > total extract > DCM-F) with a percentage (40, 71, 0%). In the light of these results; the petroleum ether fraction is the most active fraction as it has a rapid onset and longer duration of action.

2.4. Phytochemical analysis

Petroleum ether fraction was the most active fraction against different important parameters in the lipid profile diagnosis. In the light of these results, it was deemed interest to identify and isolate the main chemical constituent of the fraction. Oleamide, β-amyrin, ethyl palmitate, stigmasterol and β -sitosterol were isolated for the first time from *P. oleracea* seed, while oleamide (fatty acid amide hydrolase), is isolated for the first time from *Portulaca* species. On the other hand; the results of the GLC analysis of the petroleum ether fraction showed; total identified unsaponifiable matter was nearly equal (82.6%) of total composition. While, the total saponifiable matter was identified nearly equal (95.6%). Lignoceric acid was found to be the major unsaponifiable fatty acid (60%) followed by omega-3-, omega-6 and omega-9 fatty acids as 37, 21 and 16%, respectively (Table S2). Omega fatty acids identified by GC have long been considered essential to decrease plasma triacylglycerol levels by reducing production and enhancing the clearance of triacylglycerol-rich lipoproteins. Furthermore, these fatty acids have been used to treat and prevent atherosclerosis (Zapolska et al. 2015).

2.5. Biological activities of the isolated compounds

The triterpenoid glycosides from different plant sources lower serum cholesterol levels in a variety of animal models and also human subjects. This effect of terpenoids can explain the action mechanism of the isolated β-amyrin compound (Santos et al. 2012). In addition, the results are in accordance with previously published data; where the ethyl ester fatty acid possess hypolipidemic activity (Gunasekaran et al. 2013) such as; the isolated ethyl palmitate. On the other hand; antihypercholesterolemic studies of sterols were formerly reported (Aluko 2011). It is worthy noted that (Cheng et al. 2010) reported the hypolipidemic effect of chemically synthesised 9(Z)-octadecenamide with regard to serum TG, TC, LDL-C, LDL-C/HDL-C and hepatic TG, which explained the possible activity of isolated oleamide.

3. Conclusion

Petroleum ether fraction of the seed extract is the most active fraction for lowering cholesterol level and VLDL. While, the chloroform fraction is the most active fraction affecting TG

and LDL serum level and the ethylacetate fraction showed the most efficacy against HDL. Diverse compounds isolated from the petroleum ether bioactive fraction were reported to induce hypolipidemic effect by different mechanisms. This study justifies the clinical use of *P. oleraceae* seeds in case of dyslipidemia and obesity through the identification of related phytochemical profile. Additional *in vivo* studies and clinical trials would be needed to evaluate the potential use of isolated constituents in lowering lipid profile especially in case of diabetic conditions.

Disclosure statement

No potential conflict of interest was reported by the authors.

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