

Review: Natural products isolated from *Portulaca oleracea* (purslane, Ma-Chi-Xian): Focus on oleraciamides and oleracones

CHRISTIAN BAILLY

OncoWitan, Scientific Consulting Office. Lille (Wasquehal), 59290, France. Tel.: +33-622661817, ✉email: christian.bailly@oncowitan.com

Manuscript received: 21 September 2021. Revision accepted: 9 November 2021.

Abstract. Bailly C. 2021. Review: Natural products isolated from *Portulaca oleracea* (purslane, Ma-Chi-Xian): Focus on oleraciamides and oleracones. *Nusantara Bioscience* 13: 202-210. *Portulaca oleracea* L., purslane in English and Ma-Chi-Xian in Chinese, is largely used in traditional medicine to treat various diseases and conditions, including dysentery and urinary tract dysfunctions, and post-partum bleeding. It is also an edible plant with high nutritional potential. Extracts of *P. oleracea* display antioxidant, anti-inflammatory, and antiproliferative activities, associated with numerous bioactive secondary metabolites, including alkaloids, terpenoids, lignans, and polysaccharides. The present review focuses on two sub-groups of natural products isolated in recent years from *P. oleracea*: the alkaloids oleraciamides A-to-G and the oleracones A-to-L, which are mostly flavonoids. Their structural diversity and pharmacological properties, described in recent publications and patents, have been analyzed. These two subgroups of natural products deserve additional studies to delineate their mechanism of action. In addition, they could serve as a starting point for the design of novel anti-inflammatory agents, at least for some of them. This review provides a global view of these compounds, which is necessary to promote further phytochemical studies and better apprehend the traditional use of the plant and its extracts.

Keywords: Alkaloids, cancer, flavonoids, inflammatory diseases, natural products, traditional medicine

INTRODUCTION

Portulaca oleracea L. (purslane) is largely used in traditional medicine to treat various diseases and conditions. *P. oleracea* extracts are used to treat chronic cough and asthma (Khazdair et al. 2019; Moghaddam et al. 2020), gastrointestinal diseases, and hepatic disorders (Farkhondeh and Samarghandian 2019; Farkhondeh et al. 2019; Ong and Kim 2020), urological infections (Jaradat et al. 2017), uterine bleeding (Mobli et al. 2015), dysuria (Jaladat et al. 2015), wound healing (Laitiff et al. 2010), and other conditions (Niazi et al. 2018). Extracts of *P. oleracea* display marked analgesic and anti-inflammatory effects at the origin of the extensive traditional use of the plant in many countries (Chan et al. 2000). The traditional use of the plant goes back to ancient times, more than 2,000 years ago. The plant *Portulaca sylvestris* (synonym for *P. oleracea*) was cited by the Greek botanist Pedanius Dioscorides of Anazarba (ca. 40-90 C.E.) in his famous book "De Materia Medica" (Latinized title of the medical textbook which was hand-written in Greek). The book references about 600 plants, including *Andrachne*, the Greek name for *Portulaca*, the Latin name. The book mentioned the use of purslane together with axungia (animal fat) for the treatment of strumae (goiter) (Mitich 1997). Herba *Portulacae Oleraceae* seed is used in traditional Iranian medicine for alleviating a wide spectrum of diseases (Mirabzadeh et al. 2013; Iranshahy et al. 2017) and in Malaysia, where the plant is called Gelang pasir (Abu Bakar et al. 2018). The therapeutic use of the plant is mentioned in traditional Unani medicine (Sultana and

Rahman 2013; Khanam et al. 2019). The plant has been known in Italy since the Roman Age (Danin et al. 2014). In Japan, a health food marketed under the Gogyo-so-cha label, made from *P. oleracea*, treats intestinal infections and dysentery. Gogyo-so-cha efficiently inhibits the growth of intestinal pathogens, such as *Shigella dysenteriae* and *Vibrio cholerae* (Okuda et al. 2021). The plant (Figure 1) is also used in India and other countries (Masoodi et al. 2011; Kumar et al. 2021).

The plant has different names in China, mainly Mǎ Chǐ Xiàn but also Zhu Mu Ru, Gua Zi Cai, Wu Xing Cai in Shanghai, Ma Zi Cai in Shanxi and Liaoning, Suan Cai in Fujian and Suan Xian in Zhejiang province (Zhou et al. 2015). It has a variety of medical uses: to reduce the swelling and pain from a snake bite or wasp stings, to treat dysentery, urinary tract infections and dysfunctions or pain, red and white vaginal discharge, and post-partum bleeding. In traditional Chinese medicine, the plant is often combined with other medicinal plants, such as in the preparation called Zhiyang Pingfu (Figure 1), used to treat skin damage and lesions induced by specific anticancer drugs (Wang et al. 2015; Peng et al. 2017, 2019; Zheng et al. 2018). Many herbal combinations are proposed, with dandelion herb (Pu Gong Ying), *Smilax glabra* roots (Tu Fu Ling), and others. Some modern herbal preparations include *P. oleracea*, such as the seven herbal plant mixture BRM270 used to treat cancer by targeting cancer stem cells (Chandimali et al. 2020). In addition, *Portulacae oleracea* exhibits marked anti-hyperglycemic, anti-hyperlipidemic, reno-protective, and hepatoprotective effects (Khazdair et al. 2021), and in recent years the plant has also revealed

marked anticancer activities, owing to its antiproliferative and immune-modulatory properties (Azarifar et al. 2018; Rahimi et al. 2019; Alipour et al. 2021; Jia et al. 2021). The anti-obesity and antidiabetic effects of *P. oleracea* powder have been recently highlighted (Jung et al. 2021) as the hepatoprotective effects (Dar et al. 2021).

Beyond its medicinal use, *P. oleracea* is a wild edible plant with culinary and nutritional value, largely consumed in some countries (Pereira et al. 2020). The epithet *oleracea* is from Latin and means "of cultivation" or "suitable for food" (Mitich 1997; Kumar et al. 2021). The plant, widespread in temperate and tropical regions of the world, contains high amounts of omega-3 fatty acid, mineral elements (potassium and magnesium), alpha-tocopherol, ascorbic acid, and other elements of high nutritional potential (Uddin et al. 2014; Lyons et al. 2020; Melilli et al. 2020a). Purslane is highly nutritious and is considered for its major nourishing benefits in the current context of changing climate (Srivastava et al. 2021). The cultivated plant contained greater amounts of amino acids and vitamins than wild purslane. Still, on the opposite, the content of phenolic acids, flavonoids, alkaloids, and betanin was two-fold higher in the wild than in cultivated purslane (Nemzer et al. 2020). The nutritional value and utility of the plant are more and more recognized (Petropoulos et al. 2019). A recent clinical study suggested that consuming purslane supplementation would be beneficial in controlling blood lipid and glucose levels (Hadi et al. 2019). The plant can supplement bread (Melilli et al. 2020b) and other food products (including chewable tablets). A fermented *P. oleracea* juice has been proposed as a functional beverage to counteract intestinal inflammation (Di Cagno et al. 2019). An aqueous extract has been tested successfully as a nutritive anti-browning agent for fresh-cut potatoes (Liu et al. 2019).

The biologically active compounds in *P. oleracea* are extremely diversified, comprising flavonoids, cyanins, lignans, terpenes, phenolic alkaloids, and bioactive polysaccharides (Yang et al. 2009; Zhou et al. 2015; Duan et al. 2021). The plant has been known for decades, but novel natural products are regularly isolated and characterized (Nemzer et al. 2021; Park et al. 2021), such as oleralignan A (Xu et al. 2021) and oleraceins X and Y

(Fernández-Poyatos et al. 2021). Over the past 3-5 years, new alkaloids were identified called oleracimides and new flavones designated oleracones. A review of these natural products, their structural diversity, and their biological properties are presented here. These molecules have never been reviewed before; they would deserve more attention and to be better known by the phytochemistry/pharmacology community.

OLERACIAMIDE ALKALOIDS

Seven oleraciamide (OCM) alkaloids have been identified thus far, designated oleraciamides A-to-G (Figure 2). OCM A-to-E has been patented (Table 1). OCM-A and -B were isolated from *P. oleracea* in 2017 (Li et al. 2017a). They present the same di-substituted benzene core with a pivalamide (trimethylacetamide) group at position C-1 and an ethoxy group at position C-3. Still, they differ by the presence of a terminal morpholino group for OCM-A versus a (rare) dioxazepan group for OCM-B (Figure 2). OCM-A showed no cytotoxic properties, and OCM-B was not evaluated (Li et al. 2017a). The absence of a cytotoxic effect with OCM-A may be due to its low bioavailability and rapid metabolism observed in rat plasma after oral and intravenous administration of a *P. oleracea* extract. Seven metabolites were identified in the plasma and urine, corresponding to the natural product's hydrolyzation, glucuronidation, sulfation, and glutathionylation (Ying et al. 2018). It is mainly the intestinal first-pass effect that is responsible for the low bioavailability of OCM-A (5.7%) because the compound is a good substrate for cytochrome CYP3A and the efflux pump PgP (P-glycoprotein) (Zhao et al. 2019a). The compound is subject to rapid efflux, which limits intestinal absorption. The bioavailability can be considerably improved when the rectal or intraportal route administers the compound to reach a bioavailability of 92.2% (hepatic route) and 84.9% (gastric route). The rectal administration could be a suitable delivery route for this compound (Zhao et al. 2019a).

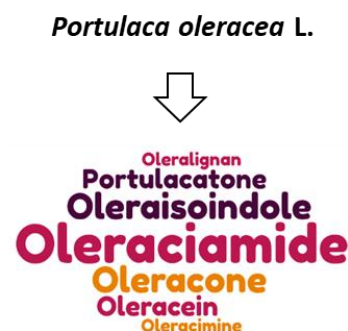


Figure 1. Illustration of the plant *Portulaca oleracea* L. (purslane, Ma-Chi-Xian) (photos from www.plantsoftheworldonline.org). Numerous natural products have been isolated from *P. oleracea*, including the oleraciamides and oleracones, reviewed here

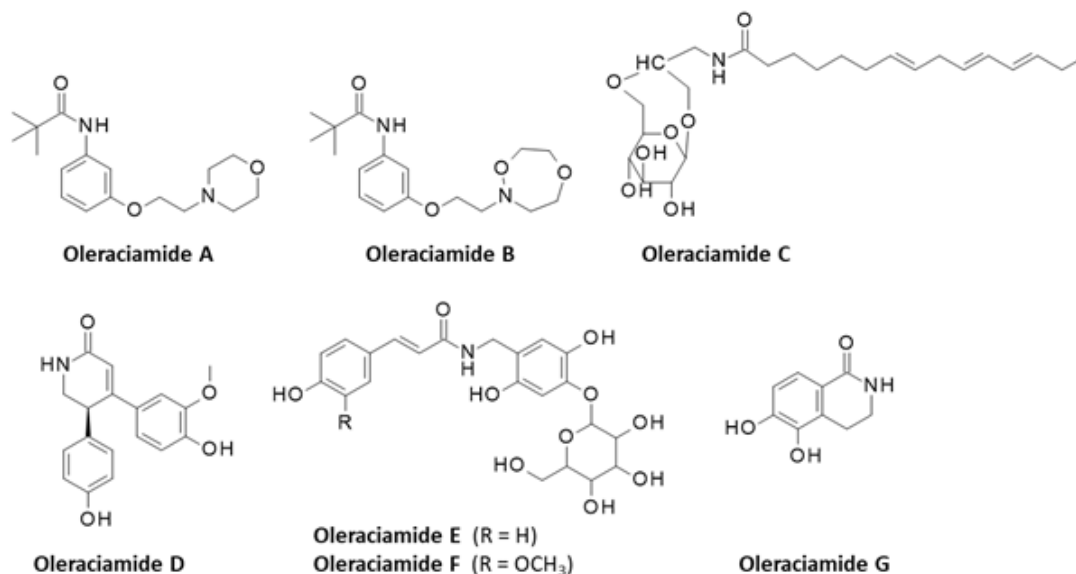


Figure 2. Structures of oleraciamide alkaloids. OCM-A (*N*-(3-(2-morpholinoethoxy)phenyl) pivalamide); OCM-B (*N*-(3-(2-(15-dioxazepan-2-yl)ethoxy)phenyl) pivalamide); OCM-C (7*E*,10*E*,12*E*)-*N*-(((1*R*,4*S*,7*R*,8*S*,9*S*,10*R*)-8,9,10-trihydroxy-2,5,11-trioxabicyclo [5.3.1]undecan-4-yl)methyl)pentadeca-7,10,12-trienamide); OCM-D ((5*R*)-4-(3-methoxy-4-hydroxyphenyl)-5-(4-hydroxyphenyl)-5,6-dihydropyridin-2(1*H*)-one); OCM-E ((*E*)-*N*-(2,5-dihydroxy-4-((3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2H-pyran-2-yl)oxy)benzyl)-3-(4-hydroxyphenyl)acrylamide); OCM-F ((*E*)-*N*-(2,5-dihydroxy-4-((3,4,5-trihydroxy-6-(hydroxymethyl)tetrahydro-2H-pyran-2-yl)oxy)benzyl)-3-(4-hydroxy-3-methoxyphenyl)acrylamide); OCM-G (5,6-dihydroxy-3,4-dihydroisoquinolin-1(2*H*)-one)

Table 1. Patent applications on oleraciamide alkaloids

Compounds	Patent numbers and titles	Registration/ publication dates
Oleraciamide A	CN106220587B	Filing: 2016-08-15
Oleraciamide B	Two kinds of alkaloid compounds and their extraction separation method in purslane	Priority: 2016-08-15 Publication (A): 2016-12-14 Application granted: 2018-05-18 Publication (B): 2018-05-18
Oleraciamide C	CN106279305B Amide alkaloid compound and its extraction separation method in purslane	Filing: 2016-08-15 Priority: 2016-08-15 Publication (A): 2017-01-04 Application granted: 2018-07-27 Publication (B): 2018-07-27
Oleraciamide D	CN106946766B Alkaloid compound and its extraction separation method in purslane	Filing: 2017-05-11 Priority: 2017-05-11 Publication (A): 2017-07-14 Application granted: 2019-07-02 Publication (B): 2019-07-02
Oleraciamide E	CN109897077A Compound Oleraciamide E and its extraction separation method and application in purslane	Filing: 2019-04-03 Priority: 2019-04-03 Publication (A): 2019-06-18

OCM-C, isolated one year later, is a different amide alkaloid possessing an unusual 1,6 bis-substituted β -glucopyranose residue linked to a long (C15) hydrophobic alkylamide side chain (Figure 2). The compound showed no cytotoxic effect but was tested against one cell line only. Even more, at low concentrations, OCM-C seemed to stimulate the growth of Human adipose-derived stem cells markedly (Xu et al. 2017). OCM-D is a tricyclic lactam alkaloid bearing a central dihydropyridinone unit substituted with two hydroxyphenyl groups (Figure 2). The compound has revealed a modest antiproliferative action against neuroblastoma SH-SY5Y cells when tested at a

concentration of 50 μ M. The compound could derive biosynthetically from the precursor of *N*-transferuloyltyramine, also isolated from *P. oleracea* (Zhao et al. 2018). This tyramine derivative (also known as moupinamide), found in diverse plants and food components (such as the traditional Chinese food Laba garlic) (Gao et al. 2019), is known for its antioxidant and antiproliferative activities (Thangnipon et al. 2012). It also shows anti-inflammatory effects, attributed to the downregulation of cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS) via suppression of transcription factors AP-1 and the JNK signaling pathway

in RAW 264.7 macrophages (Jiang et al. 2015). N-trans-feruloyltyramine and its two analogs N-trans-feruloyl-3-methoxytyramine and N-trans-coumaroyltyramine have been isolated from a *P. oleracea* extract, together with the isoindole alkaloid named oleraisoindole (Jiang et al. 2018). Diverse trans-feruloyltyramine derivatives can be found in *P. oleracea* extracts, such as 7'-ethoxy-trans-feruloyltyramine, a good antioxidant compound (Ying et al. 2020). OL-D warrants need further investigations.

The structures and properties of OCM-E and F were published one year ago (Liu et al. 2021), and OCM-E is described in a Chinese patent (CN109897077A in Table 1). They both include a feruloyl unit linked to a trihydroxyphenyl-methylamine unit connected with a β -D-glucose, and they differ by the presence or absence of a 3-methoxy substituent, as shown in Figure 2. The aglycone part shares an analogy with N-trans-feruloyltyramine but is one carbon shorter (phenyl-methylamine vs. phenyl-ethylamine). The carbohydrate unit is the same as for OCM-C (β -D-Glc). According to the patent, OCM-E displays anti-inflammatory properties, inhibiting the release of NO by LPS-stimulated RAW264.7 macrophages, as well as the production of interleukin 6 (IL-6), tumor necrosis factor- α (TNF α) and prostaglandin E₂ (PGE₂). Its antiproliferative activity is modest, with IC₅₀ varying from 20.2 to 39.1 μ M depending on the cancer cell line tested. OCM-E also inhibits the acetylcholinesterase enzyme in vitro (IC₅₀: 52.4 μ M) (Liu et al. 2021). No biological data has been reported for OCM-F. Finally, the isolation of oleraciamide G (OCM-G) from *P. oleracea* has been recently published, together with an indole alkaloid named oleraindole D (Xu et al. 2020). OCM-G is a dihydroisoquinolinone derivative endowed with a weak anticholinesterase activity (IC₅₀: 65.7 μ M), roughly like that measured with oleraindole D (IC₅₀: 58.8 μ M).

OLERACONES

Thus far, the oleracone family includes 13 compounds, designated oleracone, and oleracones A-to-L, mostly described in specific Chinese patents (Table 2) and a few publications (cited below). The patents essentially describe the compounds' isolation procedure and chemical characterization with relatively little biological information. Below, the compounds are presented in chronological order of discovery. Their chemical structures are shown in Figure 3.

The first compound in the series was named oleracone (OL). It was isolated from *P. oleracea* in 2016, and its anti-inflammatory activity was characterized in vitro. The compound was found to inhibit the production of pro-inflammatory cytokines, such as IL-6 and TNF α induced by lipopolysaccharide (LPS) in RAW264.7 macrophages (Meng et al. 2016). The compound was moderately potent, reducing nitric oxide (NO) production and PGE₂ release at 50 μ M. However, the compound showed a rapid distribution in the rat after oral administration and a satisfactory bioavailability of about 75% (Meng et al. 2016). This first compound was rapidly followed by the discovery of two molecules designated oleracones A and B, described in a parallel study combined with the alkaloids oleracimine and oleracimine A (Li et al. 2016). OL, OL-A, and OL-B are atypical bicyclic molecules (Figure 3). OL-A includes an 8-oxo-cyclopenta-azocine bicycle with an acetamide substituent. OL-B bears an atypical tetrahydroazulenone core, rarely found in nature. Unfortunately, there is very little information about this compound which has also been mentioned in a recent publication in Chinese (Sun et al. 2019).

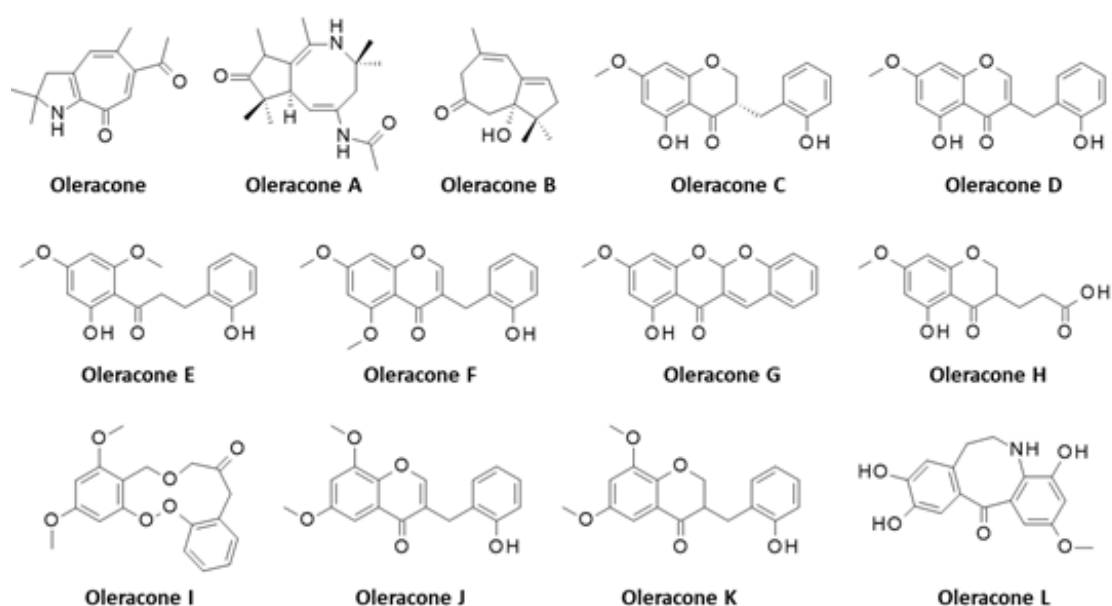


Figure 3. Structures of oleracone natural products

Table 2. Patent applications on oleracone compounds

Compounds	Patent numbers and titles	Registration/ publication dates
Oleracone	CN105330588B Alkaloid Oleracone and its extraction separation method in purslane	Filing: 2015-10-16 Priority: 2015-10-16 Publication (A): 2016-02-17 Application granted: 2017-09-26 Publication (B): 2017-09-26
Oleracone	CN105232539B Two breeds of horses' bitterroot source organism alkali are used as the application for preparing anti-inflammatory drug	Filing: 2015-10-16 Priority: 2015-10-16 Publication (A): 2016-01-13 Application granted: 2017-09-05 Publication (B): 2017-09-05
Oleracone A	CN106008502B Purslane middle skeleton alkaloid compound and its extraction separation method	Filing: 2016-06-06 Priority: 2016-06-06 Publication (A): 2016-10-12 Application granted: 2017-09-26 Publication (B): 2017-09-26
Oleracone B	CN106083556B Azulene structural compounds and its extraction separation method in purslane	Filing: 2016-06-06 Priority: 2016-06-06 Publication (A): 2016-11-09 (A) Application granted: 2018-05-18 Publication (B): 2018-05-18
Oleracone C	CN107746397B Compound Oleracone C and its extraction separation method in purslane	Filing: 2017-11-28 Priority: 2017-11-28 Publication (A): 2018-03-02 Application granted: 2019-09-17 Publication (B): 2019-09-17
Oleracone D	CN107698546B Compound Oleracone D and its extraction separation method in purslane	Filing: 2017-11-28 Priority: 2017-11-28 Publication (A): 2018-02-16 Application granted: 2019-09-17 Publication (B): 2019-09-17
Oleracone E	CN107827726A Compound Oleracone E and its extraction separation method in purslane	Filing: 2017-11-28 Priority: 2017-11-28 Publication (A): 2018-03-23
Oleracone F	CN108558809B Compound Oleracone F in purslane and extraction and separation method thereof	Filing: 2018-04-17 Priority: 2018-04-17 Publication (A): 2018-09-21 Application granted: 2020-01-21 Publication (B): 2020-01-21
Oleracone G	CN109824685A Compound oleracone G and its extraction separation method and application in purslane	Filing: 2019-04-03 Priority: 2019-04-03 Publication (A): 2019-05-31
Oleracone H	CN110194755A In purslane compound Oleracone H and its extraction separation method and its application	Filing: 2019-04-03 Priority: 2019-04-03 Publication (A): 2019-09-03
Oleracone I	CN110294733A One kind of Oleracone I of a key compound containing peroxide and its extraction separation method and application in purslane	Filing: 2019-04-03 Priority: 2019-04-03 Publication (A): 2019-10-01

Oleracone C, D, and E have been discovered recently (Yang et al. 2018a). OL-D bears a characteristic 5-hydroxy,7-methoxy-chromenone unit, whereas OL-C is the corresponding chromanone derivative. In addition, they contain both a 3-(2-hydroxy-benzyl) group. In other words, they are homoisoflavone (OL-D) and homoisoflavanone (OL-C) compounds (Figure 3). In contrast, OL-E is a dihydrochalcone, a synthetic precursor to OL-C and OL-D, with a phenol unit linked to a dimethoxy-phenol unit via a 1-propanone linker (Figure 3). The antioxidant activity of the three compounds ranks in the order OL-D > OL-E > OL-C, and a very weak anticholinesterase activity was also

reported with these compounds (IC₅₀: 60-80 μM) (Yang et al. 2018b).

Oleracone F (OL-F) only differs from OL-D by the presence of a 5-methoxy group instead of the 5-hydroxy group (Figure 3). The compound was isolated with three other homoisoflavone derivatives known as portulacanonones A, B, and C (Yang et al. 2019). An efficient synthesis of OL-D and OL-F from the commercially available chemicals 4,6-dimethoxy-2-hydroxybenzophenone and 2-(benzyloxy) benzaldehyde and via the intermediate dihydrochalcone OL-E, has been reported together with the antioxidant properties of these compounds (Yoon et al.

2019). Interestingly, in an *in vivo* assay using wild-type N2 *Caenorhabditis elegans*, a treatment with OL-E and OL-F (at 20 μM) extended the lifespan of the nematodes by 13.8 and 11.8% (Yoon et al. 2019). This effect may contribute to the anti-aging properties of the plant. Indeed, purslane ethanolic extracts can attenuate aging alternations (Ahangarpour et al. 2016).

Oleracone G (OL-G) is a tetracyclic compound with a pyrano[2,3-b]pyran scaffold. The compound is described in a recent patent (Table 2) and cited in a chemical work about the synthesis of the pyrano[2,3-b]pyran unit (Osyanin et al. 2020). Otherwise, there is little information about this compound, apart from its modest antioxidant capacity (IC_{50} : 40.1 μM in the standard DPPH (1,1-diphenyl-2-picryl-hydrazyl) assay and weak antiproliferative activities against various cancer cell lines *in vitro* (IC_{50} : 42-82 μM). In addition, OL-G exhibits modest anti-inflammatory activity *in vitro* (Duan et al. 2021). Oleracone H (OL-H) is only described in a Chinese patent (Table 2). It is a 4-chromanone derivative with a propanoic acid side chain. The compound exhibits low antiproliferative activities against different cancer cell lines *in vitro* (IC_{50} : 38-96 μM) and a slightly better antioxidant capacity than OL-G (IC_{50} : 19.8 μM).

Oleracone I (OL-I) is a strange compound with an endoperoxide bridge between the two phenyl units, delimiting a unique 11-membered central ring (Figure 3).

The compound is more cytotoxic than its congeners OL-G and OL-H, with IC_{50} values in the range of 20.3-30.9 μM against different cancer cell lines *in vitro* (but probably not very stable). OL-I dose-dependently reduces the production of inflammatory mediators such as IL-6, TNF α , NO, and PGE $_2$ by LPS-induced RAW264.7 macrophages. At the concentration of 50 μM , the production of these inflammatory mediators was almost completely suppressed (patent CN110294733A, Table 2). Oleracones J and K were isolated recently; they both showed a modest antioxidant capacity and a weak anticholinesterase effect (Duan et al. 2020). Oleracone L (OL-L) is the most recent member in the series with modes of anti-inflammatory activity *in vitro* (IC_{50} : 46 μM) (Cui et al. 2021). All these compounds deserve more studies to characterize their biological effects more deeply.

The procedures reported to isolate these compounds are generally relatively long and tedious, with multiple steps of extraction, chromatographic separations, concentrations, and final HPLC purification. An example of a process for isolating OL-G is presented in Figure 4. The compound was isolated in 6 successive steps, starting from 150 kg of dried purslane, through several chromatographic separations (the final yield was not specified in the patent CN109824685A).

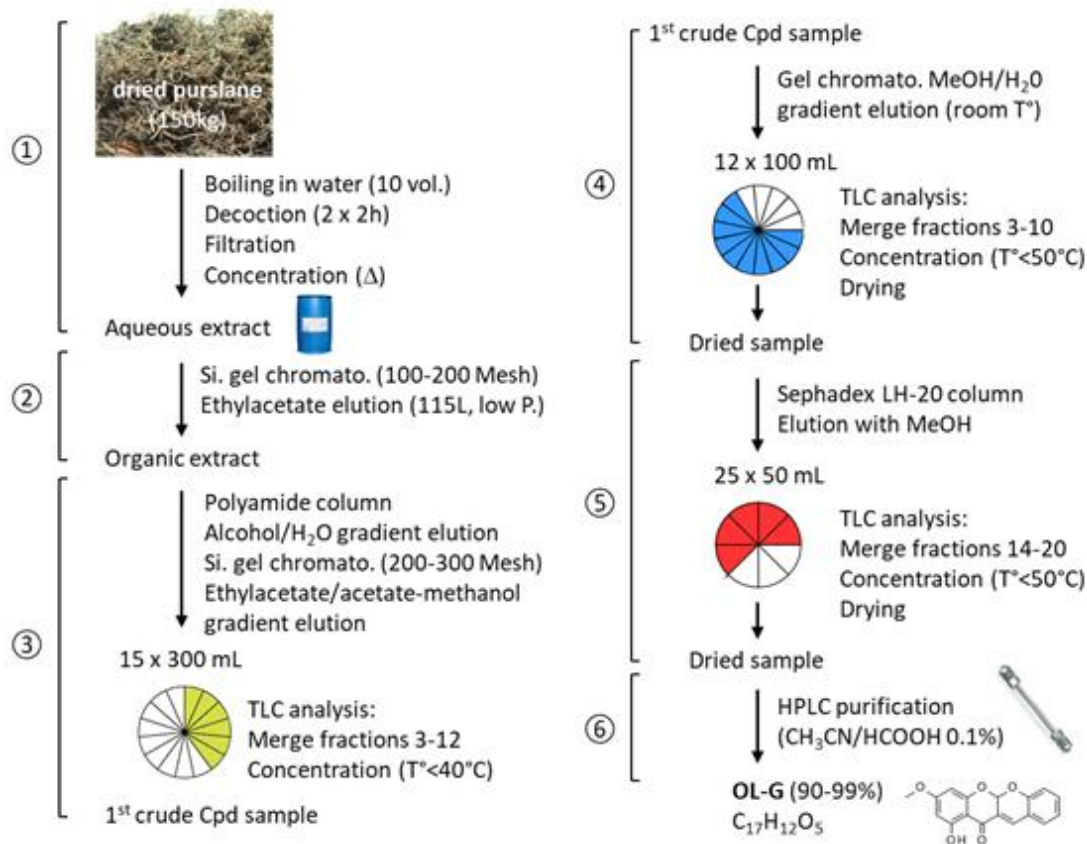


Figure 4. Summary of the purification process developed to extract and purify oleracone G (OL-G) from *Portulaca oleracea* (inferred from patent CN109824685A (Table 2). The process is divided into 6 steps, implemented one after the other, to purify OL-G starting from the dried plant. TLC, thin layer chromatography

CONCLUSION AND PERSPECTIVES

Portulaca oleracea, commonly known as purslane, is a popular plant of great value for its nutritional composition and its traditional medicinal uses in many countries. However, it also represents a reservoir of natural products, largely explored over the past thirty years but still incompletely known. A phytochemical survey of the natural products found in *P. oleracea* extracts was reported in 2015 (Zhou et al. 2015) and 2017 (Iranshahy et al. 2017). Still, over the past 3-4 years, many other new natural products have been identified from the plants. For example, we can cite the alkaloid oleraisoindole aforementioned (Jiang et al. 2018) and its hydroxylated analogue named oleroisindole A (Ma et al. 2021), the alkaloid portulacatonones A and B and portulacatal (Gu et al. 2020; Cui et al. 2021), the alkaloid 1-carbomethoxy- β -carboline (Kim et al. 2019), a series of water-soluble alkaloids called oleraceins (Fu et al. 2021), but also several homoisoflavonoids (Lee et al. 2019), the chalcone 2,4'-dihydroxy-3',5'-dimethoxychalcone (Wang et al. 2020) and chromanone derivatives such as 5,7-dimethoxy-3-(2'-hydroxybenzyl)-4-chromanone and HM-chromanone (Park et al. 2019; Je et al. 2021; Kang et al. 2021; Park et al. 2021), a few lignans such as oleralignans A and B (Wei et al. 2019; Duan et al. 2021) and other compounds (Miao et al. 2019; Wei et al. 2019; Xiu et al. 2019; Zhao et al. 2019b; Wang et al. 2020). Recently, metabolomic analysis of several taxa of *P. oleracea* L. has identified 85 metabolites, including the large series of cyclo-dopa alkaloids, designated oleraceins A-to-W (Farg and Shakour 2019). These products complete the panoply of compounds previously isolated from purslane, such as the oleracimines alkaloids (Li et al. 2016, 2017b). Undoubtedly, *P. oleracea* L. is one of the richest plants in bioactive secondary metabolites.

This review provides, for the first time, a focus on two sub-groups of bioactive metabolites found in *P. oleracea* extracts the oleraciamides and oleracones. It is useful to present a global view of their structures and properties even if the information available about their pharmacological properties remains very limited. Hopefully, this survey will encourage further studies of these compounds. The oleraciamide series is disparate, with 7 compounds showing little or no structural homology between them. The most interesting compound in the series is arguably OCM-E, endowed with antiproliferative and antioxidant properties (Liu et al. 2019). This compound bears a structural analogy with the recently isolated glycosylated indole alkaloid oleraindole D (Xu et al. 2020). The oleracone series is more homogeneous, apart from OL and OL-A/B, which are atypical compounds. Moreover, OL-C-to-K forms a homogenous series with bi-, tri-, and tetracyclic members. The homoflavanone derivatives OL-C and OL-K and the homoflavones OL-D, OL-F, and OL-J bear structural analogies with known biologically active compounds. For example, OL-C presents a structural homology with the homoisoflavanone deoxysappanone B 7,4'-dimethyl ether (from the dried heartwood of the medicinal plant *Caesalpinia sappan*), recently characterized as a potent anti-angiogenic compound (Chen et al. 2020) and known as a microtubule inhibitor with a nanomolar

anti-leukemic activity (Bernard et al. 2015). Antitumor homoisoflavone derivatives have also been isolated from Vietnamese coriander (*Polygonatum odoratum*) roots and shown to induce Bcl-2 phosphorylation and apoptosis (Rafi et al. 2007). Other homoisoflavonoids could be cited; they represent a relatively rare subclass of flavonoids in nature but with a large bioactivity potential (Lin et al. 2014; Abegaz and Kinfe 2019). Therefore, it would be useful to deepen the study of compounds' bioactivities and mechanisms of action, like OL-C and OL-K. Pharmacological studies with homoisoflavonoids from *P. oleracea* are now appearing, such as the study recently reported with a compound named HM-chromanone acting as an anti-adipogenesis agent (Je et al. 2021; Park et al. 2021). These products will surely deliver their secrets and mechanisms in the next few years. Hopefully, this review will encourage phytochemists and biologists to investigate these compounds further.

REFERENCES

- Abegaz BM, Kinfe HH. 2019. Naturally occurring homoisoflavonoids: Phytochemistry, biological activities, and synthesis (Part II). *Nat Prod Commun* 14: 1-20. DOI: 10.1177/1934578X19845813.
- Abu Bakar FI, Abu Bakar MF, Abdullah N, Endrini S, Rahmat A. 2018. A review of Malaysian medicinal plants with potential anti-inflammatory activity. *Adv Pharm Sci* 2018: 1-13.
- Ahangarpour A, Lamoochi Z, Fathi Moghaddam H, Mansouri SM. 2016. Effects of *Portulaca oleracea* ethanolic extract on reproductive system of aging female mice. *Int J Reprod Biomed* 14: 205-212. DOI: 10.29252/ijrm.14.3.205.
- Alipour S, Pishkar L, Chaleshi V. 2021. Cytotoxic effect of *Portulaca oleracea* extract on the regulation of CDK1 and P53 gene expression in pancreatic cancer cell line. *Nutr Cancer* 25: 1-10. DOI: 10.1080/01635581.2021.1960386.
- Azarifar A, Piri K, Maghsoudi H, Malati ZA, Roushandeh AM. 2018. Cytotoxic Effects of aqueous extract of *Portulaca oleracea* on oral cancer cell line. *Iran J Blood Cancer* 10: 20-24.
- Bernard D, Gebbia M, Prabha S, Gronda M, MacLean N, Wang X, Hurren R, Sukhai MA, Cho EE, Manolson MF, Datti A, Wrana J, Minden MD, Al-Awar R, Aman A, Nislow C, Giaever G, Schimmer AD. 2015. Select microtubule inhibitors increase lysosome acidity and promote lysosomal disruption in Acute Myeloid Leukemia (AML) cells. *Apoptosis* 20: 948-959. DOI: 10.1007/s10495-015-1123-3.
- Chan K, Islam MW, Kamil M, Radhakrishnan R, Zakaria MN, Habibullah M, Attas A. 2000. The analgesic and anti-inflammatory effects of *Portulaca oleracea* L. subsp. *Sativa* (Haw.) Celak. *J Ethnopharmacol* 73: 445-451. DOI: 10.1016/S0378-8741(00)00318-4.
- Chandimali N, Koh H, Kim J, Lee J, Park YH, Sun HN, Kwon T. 2020. BRM270 targets cancer stem cells and augments chemo-sensitivity in cancer. *Oncol Lett* 20: 103. DOI: 10.3892/ol.2020.11964.
- Chen K, Fan Y, Gu J, Han Z, Zeng H, Mao C, Wang C. 2020. In vivo screening of natural products against angiogenesis and mechanisms of anti-angiogenic activity of deoxysappanone B 7,4'-dimethyl-ether. *Drug Des Develop Ther* 14: 3069-3078. DOI: 10.2147/DDDT.S252681.
- Cui X, Ying Z, Ying X, Jia L, Yang G. 2021. Three new alkaloids from *Portulaca oleracea* L. and their bioactivities. *Fitoterapia* 154: 1-7. DOI: 10.1016/j.fitote.2021.105020.
- Danin A, Buldrini F, Bandini Mazzanti M, Bosi G. 2014. The history of the *Portulaca oleracea* aggregate in the Emilia-Romagna Po Plain (Italy) from the Roman Age to the present. *Plant Biosys* 148: 622-634. DOI: 10.1080/11263504.2013.788098.
- Dar MA, Mir PA, Masoodi MH, Alqahtani AS, Siddiqui NA, Ahmad B. 2021. Amelioration of experimental hepatotoxicity in rats by *Portulaca oleracea* Linn. from Kashmir Himalaya. *Comb Chem High Throughput Screen* 24. DOI: 10.2174/1386207324666210713104836.
- Di Cagno R, Filannino P, Vincentini O, Cantatore V, Cavoski I, Gobetti M. 2019. Fermented *Portulaca oleracea* L. juice: A novel functional beverage with potential ameliorating effects on the intestinal inflammation and epithelial injury. *Nutrients* 11: 1-18. DOI: 10.3390/nu11020248.

- Duan Y, Ying Z, He F, Ying X, Jia L, Yang G. 2021. A new skeleton flavonoid and a new lignan from *Portulaca oleracea* L. and their activities. *Fitoterapia* 153: 1-6. DOI: 10.1016/j.fitote.2021.104993.
- Duan Y, Ying Z, Zhang M, Ying X, Yang G. 2020. Two new homoisoflavones from *Portulaca oleracea* L. and their activities. *Nat Prod Res* 3: 1-9 DOI: 10.1080/14786419.2020.1815742.
- Farag MA, Shakour ZTA. 2019. Metabolomics driven analysis of 11 *Portulaca* leaf taxa as analysed via UPLC-ESI-MS/MS and chemometrics. *Phytochemistry* 161: 117-129. DOI: 10.1016/j.phytochem.2019.02.009.
- Farkhondeh T, Samarghandian S. 2019. The therapeutic effects of *Portulaca oleracea* L. in hepatogastric disorders. *Gastroenterol Hepatol* 42: 127-132. DOI: 10.1016/j.gastrohep.2018.07.016.
- Farkhondeh T, Samarghandian S, Azimi-Nezhad M, Hozeifi S. 2019. The hepato-protective effects of *Portulaca oleracea* L. extract: Review. *Curr Drug Discov Technol* 16: 122-126. DOI: 10.2174/1570163815666180330142724.
- Fernández-Poyatos MDP, Llorent-Martínez EJ, Ruiz-Medina A. 2021. Phytochemical composition and antioxidant activity of *Portulaca oleracea*: Influence of the steaming cooking process. *Foods* 10: 94. DOI: 10.3390/foods10010094.
- Fu J, Wang H, Dong C, Xi C, Xie J, Lai S, Chen R, Kang J. 2021. Water-soluble alkaloids isolated from *Portulaca oleracea* L. *Bioorg Chem* 113: 105023. DOI: 10.1016/j.bioorg.2021.105023.
- Gao X, Wang C, Chen Z, Chen Y, Santhanam RK, Xue Z, Ma Q, Guo Q, Liu W, Zhang M, Chen H. 2019. Effects of N-trans-feruloyltyramine isolated from laba garlic on antioxidant, cytotoxic activities and H₂O₂-induced oxidative damage in HepG2 and L02 cells. *Food Chem Toxicol* 130: 130-141. DOI: 10.1016/j.fct.2019.05.021.
- Gu Y, Leng A, Zhang W, Ying X, Stien D. 2020. A novel alkaloid from *Portulaca oleracea* L. and its anti-inflammatory activity. *Nat Prod Res* 21: 1-6. DOI: 10.1080/14786419.2020.1795855.
- Hadi A, Pourmasoumi M, Najafgholizadeh A, Kafeshani M, Sahebkar A. 2019. Effect of purslane on blood lipids and glucose: A systematic review and meta-analysis of randomized controlled trials. *Phytother Res* 33: 1-10. DOI: 10.1002/ptr.6203.
- Iranshahy M, Javadi B, Iranshahi M, Jahanbakhsh SP, Mahyari S, Hassani FV, Karimi G. 2017. A review of traditional uses, phytochemistry and pharmacology of *Portulaca oleracea* L. *J Ethnopharmacol* 205: 158-172. DOI: 10.1016/j.jep.2017.05.004.
- Jaladat AM, Atarzadeh F, Rezaeizadeh H, Mofid B, Mosalaie A, Farhan F, Amin G. 2015. Botanicals: An alternative remedy to radiotherapy-induced dysuria. *Complement Ther Med* 23: 90-99. DOI: 10.1016/j.ctim.2014.11.004.
- Jaradat NA, Zaid AN, Al-Ramahi R, Alqub MA, Hussein F, Hamdan Z, Mustafa M, Qneibi M, Ali I. 2017. Ethnopharmacological survey of medicinal plants practiced by traditional healers and herbalists for treatment of some urological diseases in the West Bank/Palestine. *BMC Compl Altern Med* 17: 1-18. DOI: 10.1186/s12906-017-1758-4.
- Je JY, Park JE, Seo Y, Han JS. 2021. HM-chromanone inhibits adipogenesis by regulating adipogenic transcription factors and AMPK in 3T3-L1 adipocytes. *Eur J Pharmacol* 892: 1-9.
- Jia G, Shao X, Zhao R, Zhang T, Zhou X, Yang Y, Li T, Chen Z, Liu Y. 2021. *Portulaca oleracea* L. polysaccharides enhance the immune efficacy of dendritic cell vaccine for breast cancer. *Food Funct* 12: 4046-4059. DOI: 10.1039/D0FO02522D.
- Jiang M, Zhang W, Yang X, Xiu F, Xu H, Ying X, Stien D. 2018. An isoindole alkaloid from *Portulaca oleracea* L. *Nat Prod Res* 32: 2431-2436. DOI: 10.1080/14786419.2017.1419226.
- Jiang Y, Yu L, Wang MH. 2015. N-trans-feruloyltyramine inhibits LPS-induced NO and PGE₂ production in RAW 264.7 macrophages: Involvement of AP-1 and MAP kinase signalling pathways. *Chem-Biol Interact* 235: 56-62. DOI: 10.1016/j.cbi.2015.03.029.
- Jung JH, Hwang SB, Park HJ, Jin GR, Lee BH. 2021. Antiobesity and antidiabetic effects of *Portulaca oleracea* powder intake in high-fat diet-induced obese C57BL/6 mice. *Evid Based Complement Alternat Med* 2021: 1-11. DOI: 10.1155/2021/5587848.
- Kang E, Park JE, Seo Y, Han JS. 2021. (E)-5-hydroxy-7-methoxy-3-(2'-hydroxybenzyl)-4-chromanone isolated from *Portulaca oleracea* L. suppresses LPS-induced inflammation in RAW 264.7 macrophages by downregulating inflammatory factors. *Immunopharmacol Immunotoxicol* 43 (5): 611-621. DOI: 10.1080/08923973.2021.1963271.
- Khanam B, Begum W, Tipo FA. 2019. Pharmacological profile, phytoconstituents, and traditional uses of Khurfa (*Portulaca oleracea* L.): Unani perspective. *J Pharma Innov* 8: 367-372.
- Khazdair MR, Anaeigoudari A, Kianmehr M. 2019. Anti-asthmatic effects of *Portulaca oleracea* and its constituents, a review. *J Pharmacopunct* 22: 122-130.
- Khazdair MR, Saadat S, Aslani MR, Shakeri F, Boskabady MH. 2021. Experimental and clinical studies on the effects of *Portulaca oleracea* L. and its constituents on respiratory, allergic, and immunologic disorders, a review. *Phytother Res* 2021: 1-30. DOI: 10.1002/ptr.7268.
- Kim KH, Park EJ, Jang HJ, Lee SJ, Park CS, Yun BS, Lee SW, Rho MC. 2019. 1-Carbomethoxy-beta-Carboline, derived from *Portulaca oleracea* L., ameliorates I κ s-mediated inflammatory response associated with MAPK Signaling and Nuclear Translocation of NF-kappaB. *Molecules* 24: 1-14. DOI: 10.3390/molecules24224042.
- Kumar A, Sreedharan S, Singh P, Achigan-Dako EG, Ramchiary N, 2021. Improvement of a traditional orphan food crop, *Portulaca oleracea* L. (purslane) using genomics for sustainable food security and climate-resilient agriculture. *Front Sustain Food Syst* 5: 1-16. DOI: 10.3389/fsufs.2021.711820.
- Laitiff AA, Teoh SL, Das S. 2010. Wound healing in diabetes mellitus: Traditional treatment modalities. *Clin Therapeut* 161: 359-364.
- Lee JI, Oh JH, Kong CS, Seo Y. 2019. Evaluation of anti-adipogenic active homoisoflavonoids from *Portulaca oleracea*. *Zeitschrift für Naturforschung C J Biosci* 74: 265-273. DOI: 10.1515/znc-2018-0114.
- Li CY, Ying Z, Gao M, Wei W, Hao D, Xu L, Tao X, Zhang W, Ying X, Liu J. 2017a. Two new similar alkaloids from *Portulaca oleracea* L. *Nat Prod Res* 31: 1792-1798. DOI: 10.1080/14786419.2017.1292507.
- Li CY, Meng YH, Ying ZM, Xu N, Hao D, Gao MZ, Zhang WJ, Xu L, Gao YC, Ying XX. 2016. Three novel alkaloids from *Portulaca oleracea* L. and their anti-inflammatory effects. *J Agricult Food Chem* 64: 5837-5844. DOI: 10.1021/acs.jafc.6b02673.
- Li CY, Meng YH, Ying ZM, Xu N, Hao D, Gao MZ, Zhang WJ, Xu L, Gao YC, Stien D, Ying XX. 2017b. Correction to three novel alkaloids from *Portulaca oleracea* L. and their anti-inflammatory effects. *J Agricult Food Chem* 65: 993-994. DOI: 10.1021/acs.jafc.6b05659.
- Lin LG, Liu QY, Ye Y. 2014. Naturally occurring homoisoflavonoids and their pharmacological activities. *Planta Med* 80: 1053-1066. DOI: 10.1055/s-0034-1383026.
- Liu X, Wu H, Tao X, Ying X, Stien D. 2021. Two amide glycosides from *Portulaca oleracea* L. and its bioactivities. *Nat Prod Res* 35: 2655-2659. DOI: 10.1080/14786419.2019.1660333.
- Liu X, Yang Q, Lu Y, Li Y, Li T, Zhou B, Qiao L. 2019. Effect of purslane (*Portulaca oleracea* L.) extract on anti-browning of fresh-cut potato slices during storage. *Food Chem* 283: 445-453. DOI: 10.1016/j.foodchem.2019.01.058.
- Lyons G, Dean G, Tongaiaba R, Halavatau S, Nakabuta K, Lonolona M, Susumu G. 2020. Macro- and micronutrients from traditional food plants could improve nutrition and reduce non-communicable diseases of Islanders on Atolls in the South Pacific. *Plants* 9: 942. DOI: 10.3390/plants9080942.
- Ma Y, Li X, Zhang W, Ying X, Stien D. 2021. A trace alkaloid, oleraisoindole A from *Portulaca oleracea* L. and its anticholinesterase effect. *Nat Prod Res* 35: 350-353. DOI: 10.1080/14786419.2019.1627356.
- Masoodi MH, Ahmad B, Mir SR, Zargar BA, Tabasum N. 2011. *Portulaca oleracea* L. a review. *J Pharm Res* 4: 3044-3048.
- Melilli MG, Di Stefano V, Sciacca F, Pagliano A, Bognanni R, Scandurra S, Virzi N, Gentile C, Palumbo M. 2020a. Improvement of fatty acid profile in durum wheat breads supplemented with *Portulaca oleracea* L. quality traits of purslane-fortified bread. *Foods* 9: 764. DOI: 10.3390/foods9060764.
- Melilli MG, Pagliano A, Bognanni R, Scandurra S, Di Stefano V. 2020b. Antioxidant activity and fatty acids quantification in Sicilian purslane germplasm. *Nat Prod Res* 34: 26-33. DOI: 10.1080/14786419.2018.1560291.
- Meng Y, Ying Z, Xiang Z, Hao D, Zhang W, Zheng Y, Gao Y, Ying X. 2016. The anti-inflammation and pharmacokinetics of a novel alkaloid from *Portulaca oleracea* L. *J Pharm Pharmacol* 68: 397-405. DOI: 10.1111/jphp.12526.
- Miao L, Tao H, Peng Y, Wang S, Zhong Z, El-Seedi H, Dragan S, Zengin G, Cheang WS, Wang Y, Xiao J. 2019. The anti-inflammatory potential of *Portulaca oleracea* L. (purslane) extract by partial suppression on NF-kappaB and MAPK activation. *Food Chem* 290: 239-245. DOI: 10.1016/j.foodchem.2019.04.005.
- Mirabzadeh M, Rahimi R, Sahraee Z. 2013. Evaluation of adverse events reported in traditional Iranian medicine following administration of aqueous extract of herba *Portulacace oleraceae* seed. *J Trad Chinese Med* 33: 535-537. DOI: 10.1016/S0254-6272(13)60161-2.
- Mitich LW. 1997. Common purslane (*Portulaca oleracea*). *Weed Technol* 11: 394-397. DOI: 10.1017/S0890037X00043128.
- Mobli M, Qaraaty M, Amin G, Haririan I, Hajimahmoodi M, Rahimi R. 2015. Scientific evaluation of medicinal plants used for the treatment

- of abnormal uterine bleeding by *Avicenna*. Arch Gynecol Obstetrics 292: 21-35. DOI: 10.1007/s00404-015-3629-x.
- Moghaddam SGM, Kianmehr M, Khazdair MR. 2020. The possible therapeutic effects of some medicinal plants for chronic cough in children. Evid Based Compl Altern Med 2020: 1-15. DOI: 10.1155/2020/2149328.
- Nemzer B, Al-Taher F, Abshiru N. 2020. Phytochemical composition and nutritional value of different plant parts in two cultivated and wild purslane (*Portulaca oleracea* L.) genotypes. Food Chem 320: 1-9. DOI: 10.1016/j.foodchem.2020.126621.
- Nemzer B, Al-Taher F, Abshiru N. 2021. Extraction and natural bioactive molecules characterization in spinach, kale and purslane: A comparative study. Molecules 26: 1-13. DOI: 10.3390/molecules26092515.
- Niazi A, Rahimi VB, Soheili-Far S, Askari N, Rahmian-Devin P, Saneifar Z, Sahebkar A, Rakhshandeh H, Askari VR. 2018. A Systematic review on prevention and treatment of nipple pain and fissure: Are they curable? J Pharmacopunct 21: 139-150.
- Okuda S, Wajima T, Yamada T, Nakaminami H, Ikoshi H, Noguchi N. 2021. In vitro growth-inhibitory effects of *Portulaca oleracea* L. formulation on intestinal pathogens. Access Microbiol 3: 1-7. DOI: 10.1099/acmi.0.000208.
- Ong HG, Kim YD. 2020. Medicinal plants for gastrointestinal diseases among the Kuki-Chin ethnolinguistic groups across Bangladesh, India, and Myanmar: A comparative and network analysis study. J Ethnopharmacol 251: 1-14. DOI: 10.1016/j.jep.2019.112415.
- Osyenin VA, Osipov DV, Semenova IA, Korzhenko KS, Lukashenko AV, Demidov OP, Klimochkin YN. 2020. Eco-friendly synthesis of fused pyrano[2,3-*b*]pyrans via ammonium acetate-mediated formal oxa-[3 + 3]cycloaddition of 4*H*-chromene-3-carbaldehydes and cyclic 1,3-dicarbonyl compounds. RSC Adv 10: 34344-34354. DOI: 10.1039/D0RA06450E.
- Park J, Park JE, Seo YW, Han JS. 2019. 5,7-Dimethoxy-3-(2'-hydroxybenzyl)-4-chromanone inhibits α -glucosidase in vitro and alleviates postprandial hyperglycemia in diabetic mice. Eur J Pharmacol 863: 1-7. DOI: 10.1016/j.ejphar.2019.172683.
- Park JE, Seo Y, Han JS. 2021. HM-chromanone, a component of *Portulaca oleracea* L., stimulates glucose uptake and glycogen synthesis in skeletal muscle cell. Phytomedicine 83: 1-8. DOI: 10.1016/j.phymed.2021.153473.
- Peng Y, Li Q, Zhang J, Shen W, Zhang X, Sun C, Cui H. 2019. Update review of skin adverse events during treatment of lung cancer and colorectal carcinoma with epidermal growth receptor factor inhibitors. Biosci Trends 12: 537-552. DOI: 10.5582/bst.2018.01246.
- Peng YM, Cui HJ, Liu Z, Jing FF, Chu YP, Bai YP, Liu DW, Song YZ, Duan H, Qiu YQ. 2017. Treatment of EGFRs-related skin adverse reactions by Zhiyang Pingfu Lotion. Zhongguo Zhong Xi Yi Jie He Za Zhi 37: 149-154.
- Pereira AG, Fraga-Corral M, García-Oliveira P, Jimenez-Lopez C, Lourenço-Lopes C, Carpena M, Otero P, Gullón P, Prieto MA, Simal-Gandara J. 2020. Culinary and nutritional value of edible wild plants from Northern Spain rich in phenolic compounds with potential health benefits. Food Funct 11: 8493-8515. DOI: 10.1039/D0FO02147D.
- Petropoulos SA, Fernandes A, Dias MI, Vasilakoglou IB, Petrotos K, Barros L, Ferreira ICFR. 2019. Nutritional value, chemical composition and cytotoxic properties of common purslane (*Portulaca oleracea* L.) in relation to harvesting stage and plant part. Antioxidants 8: 1-15. DOI: 10.3390/antiox8080293.
- Rafi MM, Vastano BC. 2007. Identification of a structure specific Bcl-2 phosphorylating homoisoflavone molecule from Vietnamese coriander (*Polygonatum odoratum*) that induces apoptosis and G2/M cell cycle arrest in breast cancer cell lines. Food Chem 104: 332-340. DOI: 10.1016/j.foodchem.2006.11.045.
- Rahimi VB, Ajam F, Rakhshandeh H, Askari VR. 2019. A Pharmacological review on *Portulaca oleracea* L.: Focusing on anti-inflammatory, antioxidant, immuno-modulatory and antitumor activities. J Pharmacopunct 22: 7-15.
- Srivastava R, Srivastava V, Singh A. 2021. Multipurpose benefits of an underexplored species purslane (*Portulaca oleracea* L.): A critical review. Environ Manag 2021: 1-11. DOI: 10.1007/s00267-021-01456-z.
- Sultana A, Rahman K. 2013. *Portulaca oleracea* Linn: A global panacea with ethnomedicinal and pharmacological potential. Int J Pharm Pharmaceut Sci 5: 33-39.
- Sun DX, Guo XF, A LT, Ma XL, Wei HY, Ma GX, Shi LL, Zhang J. 2019. Chemical constituents from green walnut husks and their antitumor activity in vitro. Zhongguo Zhong Yao Za Zhi 44: 2278-2282.
- Thangnipon W, Suwanna N, Kitiyanant N, Soi-Ampornkul R, Tuchinda P, Munyoo B, Nobsathian S. 2012. Protective role of N-trans-feruloyl tyramine against β -amyloid peptide-induced neurotoxicity in rat cultured cortical neurons. Neurosci Lett 513: 229-232. DOI: 10.1016/j.neulet.2012.02.047.
- Uddin MK, Juraimi AS, Hossain MS, Nahar MA, Ali ME, Rahman MM. 2014. Purslane weed (*Portulaca oleracea*): A prospective plant source of nutrition, omega-3 fatty acid, and antioxidant attributes. Sci World J 2014: 1-6. DOI: 10.1155/2014/951019.
- Wang HY, Zou C, Cui HJ, Bai YP, Li Y, Tan HY, Wang W, Ju H. 2015. Treatment of epidermal growth factor receptor inhibitors associated adverse skin reactions by Zhiyang Pingfu Liquid: A clinical study. Zhongguo Zhong Xi Yi Jie He Za Zhi 35: 820-822.
- Wang Z, Yang R, Li P, Yang Z, Ling R, Shen T, Peng W, Yang Q, Yan J. 2020. A homoisoflavonoid and a fatty acid in common purslane (*Portulaca oleracea* L.) synergistically inhibit growth of *Spodoptera litura* larvae. Pest Manag Sci 76: 1513-1522. DOI: 10.1002/ps.5668.
- Wei RR, Ma QG, Zhong GY, Yang M, Sang ZP. 2019. Identification of benzisoquinolinone derivatives with cytotoxicities from the leaves of *Portulaca oleracea*. Zeitschrift für Naturforschung C J Biosci 74: 139-144. DOI: 10.1515/znc-2018-0151.
- Xiu F, Ying Z, Ying X, Yang G. 2019. Pharmacokinetic studies of soykalkoid A from *Portulaca oleracea* L. using ultra-high-performance liquid chromatography-electrospray ionization quadrupole-time of flight mass spectrometry and its antioxidant activity. Biomed Chromato 33: 1-24. DOI: 10.1002/bmc.4399.
- Xu L, Ying Z, Wei W, Hao D, Wang H, Zhang W, Li C, Jiang M, Ying X, Liu J. 2017. A novel alkaloid from *Portulaca oleracea* L. Nat Prod Res 31: 902-908. DOI: 10.1080/14786419.2016.1253081.
- Xu W, Wang J, Ju B, Lan X, Ying X, Stien D. 2021. Seven compounds from *Portulaca oleracea* L. and their anticholinesterase activities. Nat Prod Res 30: 1-7 DOI: 10.1080/14786419.2021.1916928.
- Xu W, Ying Z, Tao X, Ying X, Yang G. 2020. Two new amide alkaloids from *Portulaca oleracea* L. and their anticholinesterase activities. Nat Prod Res 20: 1-7. DOI: 10.1080/14786419.2020.1739040.
- Yang X, Ying Z, He F, Ying X, Yang G. 2018b. A pharmacokinetic study on oleracone C after oral and intravenous administration. Fitoterapia 131: 44-49. DOI: 10.1016/j.fitote.2018.10.005.
- Yang X, Ying Z, Liu H, Ying X, Yang G. 2019. A new homoisoflavone from *Portulaca oleracea* L. and its antioxidant activity. Nat Prod Res 33: 3500-3506. DOI: 10.1080/14786419.2018.1484465.
- Yang X, Zhang W, Ying X, Stien D. 2018a. New flavonoids from *Portulaca oleracea* L. and their activities. Fitoterapia 127: 257-262. DOI: 10.1016/j.fitote.2018.02.032.
- Yang Z, Liu C, Xiang L, Zheng Y. 2009. Phenolic alkaloids as a new class of antioxidants in *Portulaca oleracea*. Phytother Res 23: 1032-1035. DOI: 10.1002/ptr.2742.
- Ying Z, Jiang M, Wang L, Ying X, Yang G. 2020. Bioactivities of 7'-ethoxy-trans-feruloyltyramine from *Portulaca oleracea* L. and its metabolism in rats using ultra-high-performance liquid chromatography electrospray coupled with quadrupole time-of-flight mass spectrometry. Indian J Pharmacol 52: 130-133. DOI: 10.4103/ijp.IJP_171_18.
- Ying Z, Li C, Gao M, Ying X, Yang G. 2018. Pharmacokinetics and metabolism of olerciamide A from *Portulaca oleracea* L. in rats by UHPLC-UV and UHPLC-ESI-Q-TOF/MS. Biomed Chromato 32: 1-24. DOI: 10.1002/bmc.4061.
- Yoon JA, Lim C, Cha DS, Han YT. 2019. Synthesis and evaluation of the lifespan-extension properties of oleracones D-F, antioxidative flavonoids from *Portulaca oleracea* L. Appl Sci 9: 1-7. DOI: 10.3390/app9194014.
- Zhao C, Ying Z, Hao D, Zhang W, Ying X, Yang G. 2019a. Investigating the bioavailabilities of olerciamide A via the rat's hepatic, gastric and intestinal first-pass effect models. Biopharm Drug Dispos 40: 112-120. DOI: 10.1002/bdd.2175.
- Zhao C, Ying Z, Tao X, Jiang M Ying X, Yang G. 2018. A new lactam alkaloid from *Portulaca oleracea* L. and its cytotoxicity. Nat Prod Res 32: 1548-1553. DOI: 10.1080/14786419.2017.1385022.
- Zhao C, Zhang C, He F, Zhang W, Leng A, Ying X. 2019b. Two new alkaloids from *Portulaca oleracea* L. and their bioactivities. Fitoterapia 136: 1-5. DOI: 10.1016/j.fitote.2019.05.005.
- Zheng SY, Shen W, Peng YM, Cui HJ, Duan H, Qiu YQ, Li Q, Zhang JY, Sun CY, Zhang X. 2018. Treatment of severe rash caused by crizotinib with both traditional Chinese medicine and Western medicine: Two case reports and literature review. Med (Baltimore) 97: 1-8. DOI: 10.1097/MD.00000000000013088.
- Zhou YX, Xin HL, Rahman K, Wang SJ, Peng C, Zhang H. 2015. *Portulaca oleracea* L.: A review of phytochemistry and pharmacological effects. Biomed Res Int 2015: 1-11. DOI: 10.1155/2015/925631.