Glucosinolates (GSs)

Subjects: Others

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Glucosinolates, anionic plant secondary metabolites shared in order Brassicales together with Glucosinolates Hydrolysis Products have recently gained much focus due to their biological activities and mechanisms of action. We reviewed from various scientific databases, the health benefits of GSs/GSHPs, approaches to improve plant contents, their bioavailability, and bioactivity. Findings indicate these compounds (natural, pure, synthetic, and derivatives) play an important role in human/animals (disease therapy and prevention), plant health (defense chemicals, biofumigants/biocides), and food industries (preservatives). Overall, much interest focuses on *in vitro* studies as anti-cancers and antimicrobials. In plant, GSs/GSHPs improvement utilizes mostly biotic/abiotic stresses and short periods of phytohormones application. Their availability and bioactivity are directly proportional to their contents at the source which is affected by methods of food preparation, processing, and extraction. We, conclude that, to a greater extent, there is a need to explore and improve GSs rich sources, and these should be emphasized to obtain natural bioactive compounds/ active ingredients that can be included among synthetic and commercial products for use in maintaining and promoting health. Furthermore, the development of advanced researches on compounds pharmacokinetics, their molecular mode of action, genetics-based on biosynthesis, their uses in promoting the health of living organisms is highlighted.

Keywords: glucosinolates ; glucosinolate hydrolysis products ; natural compounds ; secondary metabolites ; bioactivity ; improvement ; bioavailability

1. Introduction

Glucosinolates (GSs) are natural, sulfur-rich anionic secondary metabolites, widely distributed in plants of the order Brassicales [1], mainly in the angiosperms families like *Brassicaceae*. Together with glucosinolate hydrolysis products (GSHPs), they are collectively described as mustard oil glucosides [2]. Only about 137 GSs have been characterized so far in plants [3]. Their core structure is composed of a β-D-glucosyl residue linked by a sulfur atom to a *cis*-N-hydroxyminosulfate ester, and a variable R group derived from a modified amino acid chain (which is the precursor used to group GSs into distinct classes). In plants, GS/GSHP compounds determine the distinct aroma, pungent flavors, and taste of foods [1].

GSs normally exist as intact compounds localized in vacuoles of different cell types. They are degraded to GSHPs by an endogenous glycosylated thioglucosidases enzyme known as myrosinase, which is physically separated in vacuoles of myrosin cells [4]. Myrosinase is activated upon cell disruption (e.g., during plant injury, feeding by herbivore/insects), metabolism by gut bacteria [5]; usually in the presence of water. The enzyme hydrolyzes GSs thioglucoside bond producing glucose, sulfate and unstable aglycone moieties which are spontaneously rearranged to either isothiocyanates (ITCs), thiocyanates, epithionitriles, nitriles and oxazolidines, among others [1][3]. The type of GSHP compounds formed depends on the nature of the GS, reaction conditions (e.g., pH, ions) and presence of other compounds such as ascorbic acid and epithiospecifier proteins [6].

As natural chemicals that facilitate defense responses against different types of stresses (biotic and abiotic) in plant [7], GSs/GSHPs, have other diverse functions that have caused them to quickly gain in popularity as a subject of growing scientific interest. Plants utilize the GSs-myrosinase system, the “mustard oil bomb” [8] as a self-defense system against microbes and herbivores [9], and lowering of myrosin cell activity makes plants more susceptible to predators and insects like aphids [4]. In addition, compounds released from the hydrolysis of intact GSs by myrosinase enzymes are used as biocides/biofumigants in agriculture. Pharmacological studies have also shown that GSs/GSHPs have supplemental health promoting/beneficial properties as anti-inflammatory, antimicrobial, antioxidant, cholinesterase inhibitors and as cancer preventive agents in humans, while in the food industry these compounds are used in food preservation owing to their microbial inhibitory ability [10].

The majority of the biological activities of GSs are linked to their GSHPs [11], however, intact GSs also have the capability of modulating and impacting some biological systems [12]. These activities may be enhanced by the availability of more than one compound which display synergetic mode of action between or with other compounds [13]. Certain other factors which affect the bioactivity of these compounds include the plants' GSs profiles (concentration and composition) [14] and hydrolysis enzyme actions [15]. Variations in plants' GSs profiles and enzyme activity may occur among genotypes [16], cultivars, organs [17], accessions [18], varieties [19][20], growth stage and depending on environmental or growth conditions like photoperiods [21], temperature, water, nutrient availability.

2. Development

Besides the naturally available sources of GSs, recently, the prediction of new, efficient bioactive GSs/GSHPs and their derivatives have been evaluated. Among them include ITC derivatives with higher antimicrobial activity [22], chemopreventive properties [23], herbicidal activity [24], antimicrobial activity [25], anti-tumor activity [26], ITCs with moderate anti-inflammatory[27][28][29] and ITCs with similar anti-proliferative activity as natural ITCs [30].

Furthermore, improvement strategies of natural GSs/GSHPs compounds using elicitors or biotic and abiotic stresses; which influence concentration, biological activity, GSs-myrosinase enzyme action, have also been assessed. In response to such factors, it has been shown that the expression profiles of various transcription factors related to GSs biosynthesis differ in various genotypes, which can be used to provide genetic diversity as well as phenotypic diversity in the GSs content [31].

Through the exploration of several studies, this review aims at providing up to date information on health benefits of different types of GSs/GSHPs, and the factors that affect their natural occurrence and bioavailability, for the various beneficial health roles they possess; so as to help in investigating the therapeutic values of these compounds in future.

3. Conclusions

GSs/GSHPs offer a wide variety of health benefits, including disease prophylactic and therapeutic effects. This review shows the usefulness of these compounds in preventing and reducing disease progression in humans and animals, their biocidal, biofumigation capabilities in plants, and their antimicrobial use in the food industry as food preservatives.

Although their composition and concentration vary in various crop species, organs, cultivars, and at different stages of development, sometimes in response to both abiotic and biotic factors, strategies to improve specific compounds have been successful, leading to improved crop varieties with both nutritional and pharmacological benefits. Biological activity assays on GSs-rich extracts exhibit a positive correlation between concentrations of GSs/GSHPs-related benefits in organisms. Taking this into consideration, the bioavailability of these compounds should be well maintained in their sources through choosing and having handling, preparative techniques, extraction methods that maintain them.

This review also reveals the necessity to maintain GSs content as bioactive compounds, to explore and improve GSs rich plant as a source of these natural compounds, which have potential as active ingredients among synthetic and commercial products to maintain and promote health. Considering that most research evaluating these natural compounds mainly focuses on the plant of *Brassicaceae* family, there is furthermore a need to probe the compounds even more *in vivo* studies, to understand their primary mechanism of actions and their molecular targets should also be emphasized.

References

1. Clarke, D.B. Glucosinolates, structures and analysis in food. Anal. Methods 2010, 2, 310–325.
2. Heldt, H.-W.; Piechulla, B. Secondary metabolites fulfill specific ecological functions in plants. Plant Biochem. 2011, 39 9–408.
3. Blažević, I.; Montaut, S.; Burčul, F.; Olsen, C.E.; Burow, M.; Rollin, P.; Agerbirk, N. Glucosinolate structural diversity, ide ntification, chemical synthesis and metabolism in plants. Phytochemistry 2020, 169, 112100.
4. Borgen, B.H.; Ahuja, I.; Thangstad, O.P.; Honne, B.I.; Rohloff, J.; Rossiter, J.T.; Bones, A.M. “Myrosin cells” are not a pr erequisite for aphid feeding on oilseed rape (Brassica napus) but affect host plant preferences. Plant Biol. 2012, 14, 89 4–904.
5. Luang-In, V.; Narbad, A.; Nueno-Palop, C.; Mithen, R.; Bennett, M.; Rossiter, J.T. The metabolism of methylsulfinylalkyl- and methylthioalkyl-glucosinolates by a selection of human gut bacteria. Mol. Nutr. Food Res. 2014, 58, 875–883.

6. Saladino, F.; Bordin, K.; Luciano, F.B.; Franzón, M.F.; Mañes, J.; Meca, G. Glucosinolates. Glucosinolates 2016.
7. Miao, H.; Wang, J.; Cai, C.; Chang, J.; Zhao, Y.; Wang, Q. Accumulation of Glucosinolates in Broccoli. In Glucosinolate s; Mérillon, J.M., Ramawat, K.G., Eds.; Springer International Publishing: New York, NY, USA, 2017; pp. 431–461.
8. Ahuja, I.; Van Dam, N.M.; Winge, P.; Trælnes, M.; Heydarova, A.; Rohloff, J.; Langaas, M.; Bones, A.M. Plant defence r esponses in oilseed rape MINELESS plants after attack by the cabbage moth Mamestra brassicae. J. Exp. Bot. 2015, 6 6, 579–592.
9. Falk, K.L.; Kästner, J.; Bodenhausen, N.; Schramm, K.; Europe PMC Funders Group. The role of glucosinolates and th e jasmonic acid pathway in resistance of Arabidopsis thaliana against molluskan herbivores. Mol. Ecol. 2016, 23, 1188 –1203.
10. Borges, A.; Abreu, A.C.; Ferreira, C.; Saavedra, M.J.; Simões, L.C.; Simões, M. Antibacterial activity and mode of actio n of selected glucosinolate hydrolysis products against bacterial pathogens. J. Food Sci. Technol. 2015, 52, 4737–474 8.
11. Abdull Razis, A.F.; Noor, N.M. Sulforaphane is Superior to Glucoraphanin in Modulating Carcinogen-Metabolising Enzy mes in Hep G2 Cells. Asian Pacific J. Cancer Prev. 2013, 14, 4235–4238.
12. Abdull Razis, A.F.; Bagatta, M.; De Nicola, G.R.; Iori, R.; Ioannides, C. Intact glucosinolates modulate hepatic cytochro me P450 and phase II conjugation activities and may contribute directly to the chemopreventive activity of cruciferous v egetables. Toxicology 2010, 277, 74–85.
13. Das, N.; Berhow, M.A.; Angelino, D.; Jeffery, E.H. Camelina sativa defatted seed meal contains both alkyl sulfinyl gluco sinolates and quercetin that synergize bioactivity. J. Agric. Food Chem. 2014, 62, 8385–8391.
14. Vale, A.P.; Santos, J.; Brito, N.V.; Fernandes, D.; Rosa, E.; Beatriz, M.; Oliveira, P.P. Evaluating the impact of sprouting conditions on the glucosinolate content of Brassica oleracea sprouts. Phytochemistry 2015, 115, 252–260.
15. Carmen, S.; Tan, M.G.; Noel, M. Glucosinolates, Degradation Products and Myrosinase Activity in Raphanus sativus Li nn. Pharmacogn. J. 2019.
16. Fechner, J.; Kaufmann, M.; Herz, C.; Eisenschmidt, D.; Lamy, E.; Kroh, L.W.; Hanschen, F.S. The major glucosinolate h ydrolysis product in rocket (Eruca sativa L.), sativin, is 1,3-thiazepane-2-thione: Elucidation of structure, bioactivity, and stability compared to other rocket isothiocyanates. Food Chem. 2018.
17. Bhandari, S.R.; Kwak, J.H. Chemical composition and antioxidant activity in different tissues of brassica vegetables. M olecules 2015, 20, 1228–1243.
18. Ku, K.M.; Jeffery, E.H.; Juvik, J.A.; Kushad, M.M. Correlation of Quinone Reductase Activity and Allyl Isothiocyanate Fo rmation among Different Genotypes and Grades of Horseradish Roots. J. Agric. Food Chem. 2015, 63, 2947–2955.
19. Lee, M.K.; Chun, J.H.; Byeon, D.H.; Chung, S.O.; Park, S.U.; Park, S.; Arasu, M.V.; Al-Dhabi, N.A.; Lim, Y.P.; Kim, S.J. Variation of glucosinolates in 62 varieties of Chinese cabbage (Brassica rapa L. ssp. pekinensis) and their antioxidant a ctivity. LWT Food Sci. Technol. 2014, 58, 93–101.
20. Hahn, C.; Müller, A.; Kuhnert, N.; Albach, D. Diversity of Kale (Brassica oleracea var. sabellica): Glucosinolate Content and Phylogenetic Relationships. J. Agric. Food Chem. 2016.
21. Huseby, S.; Koprivova, A.; Lee, B.R.; Saha, S.; Mithen, R.; Wold, A.B.; Bengtsson, G.B.; Kopriva, S. Diurnal and light re gulation of sulphur assimilation and glucosinolate biosynthesis in Arabidopsis. J. Exp. Bot. 2013, 64, 1039–1048.
22. Kurepina, N.; Kreiswirth, B.N.; Mustaev, A. Growth-inhibitory activity of natural and synthetic isothiocyanates against re presentative human microbial pathogens. J. Appl. Microbiol. 2013, 115, 943–954.
23. Anderson, R.H.; Lensing, C.J.; Forred, B.J.; Amolins, M.W.; Aegerter, C.L.; Vitiello, P.F.; Mays, J.R. Differentiating Antipr oliferative and Chemopreventive Modes of Activity for Electron-Deficient Aryl Isothiocyanates against Human MCF-7 C ells. ChemMedChem 2018, 13, 1695–1710.
24. Wu, H.; Feng, J.; Lin, K.; Zhang, X. Synthesis and Herbicidal Activity of Substituted Pyrazole Isothiocyanates. Molecule s 2012, 17, 12187–12196.
25. Tang, J.; Niu, J.; Wang, W.; Huo, H.; Li, J.; Luo, L.; Cao, Y. p-Aromatic Isothiocyanates: Synthesis and Anti Plant Patho gen Activity. Russ. J. Gen. Chem. 2018, 88, 1252–1257.
26. De Santi, M.; Galluzzi, L.; Lucarini, S.; Paoletti, M.F.; Fraternale, A.; Duranti, A.; De Marco, C.; Fanelli, M.; Zaffaroni, N.; Brandi, G.; et al. The indole-3-carbinol cyclic tetrameric derivative CTet inhibits cell proliferation via overexpression of p 21/CDKN1A in both estrogen receptor-positive and triple-negative breast cancer cell lines. Breast Cancer Res. 2011, 1 3, R33.
27. Vo, Q.V.; Trenerry, C.; Rochfort, S.; Wadeson, J.; Leyton, C.; Hughes, A.B. Synthesis and anti-inflammatory activity of a romatic glucosinolates. Bioorganic Med. Chem. 2013, 21, 5945–5954.

28. Vo, Q.V.; Trenerry, C.; Rochfort, S.; Wadeson, J.; Leyton, C.; Hughes, A.B. Bioorganic & Medicinal Chemistry Synthesis and anti-inflammatory activity of indole glucosinolates. Bioorg. Med. Chem. 2014, 22, 856–864.
29. Vo, Q.V.; Rochfort, S.; Nam, P.C.; Nguyen, T.L.; Nguyen, T.T.; Mechler, A. Synthesis of aromatic and indole alpha-gluco sinolates. Carbohydr. Res. 2018, 455, 45–53.
30. Psurski, M.; Błaewska, K.; Gajda, A.; Gajda, T.; Wietrzyk, J.; Oleksyszyn, J. Synthesis and antiproliferative activity of no vel α- And β-dialkoxyphosphoryl isothiocyanates. Bioorganic Med. Chem. Lett. 2011, 21, 4572–4576.
31. Seo, M.S.; Jin, M.; Sohn, S.H.; Kim, J.S. Expression profiles of BrMYB transcription factors related to glucosinolate bio synthesis and stress response in eight subspecies of Brassica rapa. FEBS Open Bio 2017, 7, 1646–1659.