∂ OPEN ACCESS

Scholars Bulletin

Abbreviated Key Title: Sch Bull ISSN 2412-9771 (Print) | ISSN 2412-897X (Online) Scholars Middle East Publishers, Dubai, United Arab Emirates Journal homepage: <u>https://saudijournals.com</u>

Subject Category: Botany

New Insights into Recent Adaptation in the Plant Hormones and Importance of Medicinal Plants in Agriculture Sectors

Sana Razzaq^{1*}, Sanam Maqbool¹, Mohammad Ilyas², Humaira Anwar¹, Syed Shahrayz³, Nimrah Tehreem¹, Zainab Asif⁴, Komail Muhammad⁵, Tehreen Tariq⁶

¹Department of Botany, University of Agriculture Faisalabad
²Department of Botany, Abdul Wali Khan University, Mardan
³Department of Botany, Government Murray Graduate College Sialkot (Affiliated with the University of Gujrat)
⁴Department of Botany, Pir Mehr Ali Shah Arid Agriculture University, Rawalpindi
⁵Department of Botany, University of Peshawar
⁶Department of Plant Science, Quaid-e-Azam University, Islamabad

DOI: 10.36348/sb.2024.v10i06.001

| Received: 28.04.2024 | Accepted: 01.06.2024 | Published: 07.06.2024

*Corresponding author: Sana Razzaq Department of Botany, University of Agriculture Faisalabad

Abstract

Apart from traditional phytohormones, a range of short peptides known as peptide hormones have gathered more information and focus due to their role in long-range signaling and systemic control of stress adaption and development. New networks exist the crosstalk between different phytohormones under a variety of conditions, such as plant growth, development, and responses to biotic and abiotic stress. Some of the important plant hormones are auxins, gibberellins, cytokinin's, jasmonic acid (JA), salicylic acid (SA), florigen, and strigolactones (SLs). Salicylic acid (SA), a crucial plant hormone, is involved in several activities, including thermogenesis, stomatal closure, seed germination, floral induction, root initiation, and response to biotic and abiotic stresses. Organosulfur compounds are thought to cause phase II detoxifying enzymes, such as quinone reductase and glutathione S-transferase, as well as increase the activities of superoxide dismutase (SOD), glutathione reductase, and glutathione peroxidase (GPx), which gathered ultimately lead to the detoxification and elimination of carcinogens. Ginseng and ginsenosides seem to help with immunity, cancer, diabetes, CNS function, and other conditions. These therapeutic herbs offer a sensible way to treat a variety of inside illnesses that are typically regarded to be incurable.

Keywords: Plant hormones, production, organs, cytokinins, salicylic acid, strigolactones.

Copyright © 2024 The Author(s): This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License (CC BY-NC 4.0) which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use provided the original author and source are credited.

INTRODUCTION

In general, a hormone is a family of signaling molecules that influence physiology and behavior by being produced from glands in organisms and traveling to target organs via the circulatory system. Nonetheless, the word hormone is occasionally used to refer to substances that are made by cells and have an impact on neighboring or the same cell [1, 2]. These are known as plant hormones, and they act by controlling certain targeted cells biological processes either in the vicinity of their production or by moving them to other organs. Plant hormones that have been identified to date include auxins, gibberellins (GAs), cytokinins (CKs), abscisic acid (ABA), ethylene, brassinosteroids (BRs), jasmonic acid (JA), salicylic acid (SA), florigen, and strigolactones (SLs) [3, 4].

The exogenous supply of these phytohormones may have an impact on the gut microbiota, which in turn may have an impact on metabolism and other biological processes [1, 4]. It may have both positive and negative impacts on human health. Through genetic engineering, it is possible to identify the genes that microorganisms use to produce these hormones and to control how much of them are produced. Additionally, plant hormones are essential for plant-to-plant and plant-associated microbe signaling; yet, little is known about how these hormones

Citation: Sana Razzaq, Sanam Maqbool, Mohammad Ilyas, Humaira Anwar, Syed Shahrayz, Nimrah Tehreem, Zainab Asif, Komail Muhammad, Tehreen Tariq (2024). New Insights into Recent Adaptation in the Plant Hormones and Importance of Medicinal Plants in Agriculture Sectors. *Sch Bull*, *10*(6): 160-166.

160

influence interactions between plants, animals, and microbes [5, 6].

Numerous studies have demonstrated the networks of cross-talk between different phytohormones under a variety of conditions, such as plant growth, development, and responses to biotic and abiotic stress [3, 5]. Numerous plant hormones have also been shown in recent research to have a role in the systemic control of responses to environmental factors, which enhances plant fitness by long-distance transport and communication networks across plant organs. Apart from traditional phytohormones, a range of short peptides known as peptide hormones have garnered more focus due to their role in long-range signaling and systemic control of stress adaption and development [7, 8].

New Adaptations and Applications of Phytochemicals

At first, auxin was thought to be a plant hormone because of its role in attracting plants to light or gravity. Later, it was shown that auxin is chemically represented as indole-3-acetic acid. It was also shown that auxin is essential for numerous physiological and developmental processes in plants, such as tropical growth, fruit production, vascular differentiation, embryogenesis, and root and shoot development [9, 10].

Auxin-responsive genes' function in the body's reaction to biotic stress. In order to identify the possible function of auxin in defensive responses in plants, the expression of auxin-responsive genes at the molecular level in Orvza sativa under a variety of biotic stress conditions. The geographical and temporal patterns of auxin-dependent developmental reprogramming are determined by patterns of variable auxin accumulation within a field of cells [11, 12]. However, the interpretation of these auxin accumulations at the individual cell level ultimately determines the type of developmental output. Even while auxin elicits a wide range of cellular responses, most of its actions are attributed to a single, quite straightforward mechanism that directly affects transcriptional control. Auxin signaling is essentially driven by the interaction between two kinds of transcriptional regulators [10, 13].

Auxin is transported by two different but related systems in higher plants: the first is a quick, nondirectional flow in the phloem with photo assimilates, and the second is a slow, directed intercellular polar auxin transport (PAT). The directed active movement of auxin molecules in plant tissues, known as polar transport, requires certain carrier proteins to be completed. Local hormone maxima are produced by the simultaneous action of auxin influx and efflux carrier proteins. Essential plant developmental processes including organ development, apical hook creation, gravitropism and hydrotropism bending to directed root growth, and phototropism depend on the directional auxin gradients [14, 15].

In order to activate defensive responses against biotrophic diseases and increase plant tolerance to various pathogens, salicylic acid functions as an essential endogenous signal for SAR [15]. However, it was also thought that SA activates a number of pathways, such as CDPK (calcium-dependent protein kinase), MAPK (mitogen-activated protein kinase), and other protein kinases, thereby encouraging the production of secondary metabolites in plants, which are essential for plant-pathogen interactions. Deficits in nutrients and water can also result in some effects that are similar to those brought on by infections. For instance, it was noted that Sempervivum tectorum L. were free of visual infections, and that there was a high positive correlation between the amount of SA and the relative water content and leaf hydration. It is plausible that antagonistic interactions between ABA and SA might regulate certain features of morphological alterations brought on by a water deficit [16, 17].



Fig-1: Various functions of salicylic acid with potential targets

Using a high-throughput screen, the identified many members of the Arabidopsis glyceraldehyde 3phosphate dehydrogenase (GAPDH) family, including GAPDHC1. GAPDH is necessary for plants and animals to be able to glycolyze. Invasive viruses, however, have the ability to take over many GAPDH family members in order to facilitate their replication. For instance, tomato bushy stunt virus (TBSV) cannot replicate well unless GAPDH binds to the 3' end of the negative-strand RNA template [14, 15]. As a result, the positive strand may be synthesized and translated, or packed, into the virion. Salicylic acid (SA), a crucial plant hormone, is involved in several activities, including thermogenesis, stomatal closure, seed germination, floral induction, root initiation, and response to biotic and abiotic stresses. Its vital role in plant immunity is still not fully understood, despite much research. Using conventional biochemical techniques and, more recently, genome-wide highthroughput screens, more than two dozen plant SAbinding proteins (SABPs) as well as other uncharacterized candidates have been discovered. Certain proteins have a low affinity for SA, whereas others have a high affinity. Given that the location, timing, and kind of external stimuli, as well as developmental stage, tissue type, and subcellular localization, can all have a substantial impact on SA levels, even within the same plant species [17-19].



Fig-2: Shows the various list Medicinals with potential effects

Importance of Medicinal Plants in Agriculture Sectors

Allium cepa, one of the most significant condiment plants cultivated and consumed worldwide, was studied for its many pharmacological and medicinal properties. It is a perennial plant in the Amaryllidaceae family that is rich in dietary fiber [20]. In addition to vitamins and minerals, it has a high concentration of folic acid, vitamin B6, magnesium, calcium, potassium, and phosphorus. In addition to its widespread usage as an antibacterial, this compound has been shown to have neuroprotective, anti-inflammatory, antiparasitic, antioxidant, anticancer, antiplatelet, antihypertensive, and antidepressant properties. It is claimed to have positive benefits on the immune system in addition to the respiratory, circulatory, and digestive systems. Herbaceous onions (Allium cepa L.) and garlics (Allium sativum L.) are two of the first plants purposely grown for food and medial [21, 22]. The vegetable onion has a long history of use in medicine; the bulbs are used as flavoring and for therapeutic reasons in cookery. Likewise, the roots, stalk, and leaves can be added to meals and have medicinal use. The traditional medicinal applications of onions, such as diuretics, antiarteriosclerosis by lowering blood LDL cholesterol,

and the formation of blood clots after tissue injury, have been beneficial to the circulatory system [20-22].

The effects of onions and associated components in preventing cancer have been explained by a number of different ways. For instance, quercetin can inhibit the activity of tyrosine kinases that are carcinogenic and prevent DNA damage and mutations from ROS. It can also increase the bioavailability of certain anti-cancer medications like tamoxifen by enhancing intestinal absorption and lowering metabolism [23, 24]. Organosulfur compounds are thought to cause phase II detoxifying enzymes, such as quinone reductase and glutathione S-transferase, as well as increase the activities of superoxide dismutase (SOD), glutathione reductase, and glutathione peroxidase (GPx), which will ultimately lead to the detoxification and elimination of carcinogens. Additionally, these substances influence sulfhydryl/disulfide exchange processes and cause apoptosis, both of which are likely essential for limiting tumor development and cell proliferation. Onion has anti-diabetic properties, according to the research that is currently available. Using onions to cure diabetes and reduce blood glucose levels is one of the most significant uses of onions in traditional medicine [24-26]. Onion extracts also normalize the plasma level of fat and glucose and modify the activities of liver hexokinase, glucose 6-phosphatase, and HMG coenzyme-A reductase. Patients with diabetes experience hypoglycemia after eating onions. Red onion extract treatment reduced fasting blood glucose (FBG) and enhanced glycation end products (AGEs) in streptozotocin (STZ)-induced diabetic mice. Due to hyperglycemia, treated rats with the extract also showed increased serum insulin levels and suppressed inflammatory mRNA expression [27, 28].



Fig-3: Shows the plant bioactive compounds

Reactive oxygen species (ROS), free radicals can be produced by both endogenous and external sources. Air pollution, alcohol, tobacco use, smoking, heavy metals, transition metals, industrial solvents, pesticides, and some drugs, such as paracetamol and radiation therapy, are important external contributors [29]. Examples of endogenous sources include mitochondria, phagocytic cells, peroxisomes, and the endoplasmic reticulum. Free radicals and a variety of diseases, including as senile dementia, diabetes, inflammatory joint disease, cancer, atherosclerosis, and degenerative eye disease, have been closely linked in several studies. The capacity of ginseng leaf extracts in methanol and ethanol to scavenge free radicals. In ApoEknockout mice, total Panax notoginsenosides has been demonstrated to prevent atherosclerosis, and P. notoginseng saponins lower atherosclerosis via regulating the lipid through their anti-inflammatory characteristics [30, 31]. By modifying the adenosine triphosphate-binding cassette transporter A1, saponins from P. notoginseng have the ability to reduce cholesterol ester in foam cells. Furthermore, in ApoEmice, ginsenoside Rd protected knockout atherosclerosis. P. ginseng may have antihyperlipidemic properties [31, 32].

Ginsenosides protect against myocardial reperfusion injury by reducing lipid peroxidation and increasing the production of 6-keto-prostaglandin F1 α . The rabbit pulmonary endothelium was shielded from ROS damage by ginsenosides [33, 34]. Moreover,

ginseng prevented ROS damage by encouraging the production of NO. Endothelial dysfunction was brought on by homocysteine and human immunodeficiency virus protease inhibitors, but both could be successfully avoided by ginsenoside Rb1 and other ginsenosides by reducing the production of ROS [33, 34]. Strong antioxidant ginsenoside Re protects cardiomyocytes against oxidative injury. This protection stems, at least in part, from its capacity to scavenge radicals, especially hydroxyl and H2O2 radicals. The antioxidant qualities of ginseng extract, which extend the life of cardiomyocytes and enhance their contractile function, may be mostly attributed to ginsenoside Re. Minerals, amino acids, saponins, and other water-soluble low- and highmolecular-weight compounds are all present in aqueous ginseng preparations [32-34]. It has been demonstrated that ginseng extract controls the production of cytokines in a mouse model suffering from lung Pseudomonas aeruginosa infection. The lung cells treated with ginseng extract produced higher IFN-y/IL-4 ratios, increased levels of interferon γ (IFN- γ) and tumor necrosis factor α (TNF- α), and decreased levels of interleukin 4 (IL-4). When given ginseng extract, mice with a lung infection brought on by Panax aeruginosa had indications of a Th1-like immune response [34, 35].

A range of memory-impairment models have been used to examine the effects of ginseng and its active ingredients on learning and memory. The ginsenoside Rg1 improved learning and memory consolidation, retrieval, and acquisition, indicating that Rg1 can improve memory at all stages [36, 37]. To investigate the effect of ginsenoside Rg1 on learning and memory loss caused by β -amyloid, passive avoidance and performance in the Morris water maze were assessed after the last treatment. Ginsenoside Rg1 significantly reduced latency and swimming distance, increased step-through latency, and improved corresponding changes in search strategies in the Morris water maze. In another study, Rg1 significantly reduced memory deficits in old, ovariectomized, and brain ischemia-reperfusion rats [38, 39].

Ginseng has been used as a frequent component in traditional medicine for thousands of years. Its main use has been as a general tonic and adaptogen to maintain homeostasis and the body's tolerance to outside stimuli; it also helps to improve general vitality, and physical function, and slow down the aging process. Ginseng and ginsenosides seem to help with immunity, cancer, diabetes, CNS function, and other conditions. While individual ginsenosides have been found to be beneficial for certain effects or circumstances, it is currently unknown if a single ginsenoside or mixtures of ginsengderived components can optimize benefit across a range of diseases and conditions. Therefore, more research on the relationship between the structure and activity of individual or combination ginseng components working together is required to predict [38-40].

Phospholipids may be essential in improving the therapeutic effectiveness of small molecules, especially those with limited oral bioavailability, according to a number of studies. Amphipathic phospholipid complexes frequently serve as bioactive components that enable substances to pass through the digestive system and into the circulation. In principle, phospholipid complexes can be effective strategies for any small bioactive substance [41]. The curcumin molecule has been found to have a great affinity for biological membranes and a tendency to penetrate them fast in order to form dimeric biological complexes. A phenolic compound with limited solubility, curcumin can create non-covalent adducts with phospholipids, particularly phosphatidylcholine. Curcumin has potent anti-cancer properties because, as several studies have shown, it inhibits angiogenesis, the process by which preexisting blood vessels split into new ones. Angiogenesis is a multiphase process including endothelial cell activation, proliferation, invasion, and migration. Curcumin has been shown to reduce angiogenesis repeatedly in several cancers by inhibiting these phases. Furthermore, curcumin inhibited VEGF Receptor signaling in vivo to restrict lymphangiogenesis, or the development of new lymphatic vessels, a critical process in the spread of cancer [41, 42]. These can cause cancers of the gastrointestinal system. The curcuminbound chitosan nanostructures and demonstrated the efficacy of using this tactic to improve metabolic durability, biocompatibility, and bioavailability in mice as well as antimalarial activity. The efficiency of antisolvent precipitation, which is influenced by stirring speed, temperature, and time, has emerged as a further often practical and affordable technique for creating curcumin nanostructures. It also increases the stability and solubility of curcumin nanostructures. Its ease of usage makes it suitable for use in the industrial processing of medicinal nanomaterials [43, 44].

CONCLUSION

The therapeutic herbs offer a sensible way to treat a variety of inside illnesses that are typically regarded to be incurable. The curcumin molecule has been found to have a great affinity for biological membranes and a tendency to penetrate them fast in order to form dimeric biological complexes. These bioactive compounds have been shown to have neuroprotective, anti-inflammatory, antiparasitic, antioxidant, anticancer, antiplatelet, antihypertensive, and antidepressant properties. Because there are medicinal plant treatments are regarded as being quite use. The biggest benefit is that these treatments are in harmony with nature.

REFERENCES

- 1. Davies, P. J. (2010). The plant hormones: their nature, occurrence, and functions Plant Hormones pp. 1-15, 10.1007/978-1-4020-2686-7_1
- 2. Jiang, K., & Asami, T. (2018). Chemical regulators of plant hormones and their applications in basic research and agriculture. *Bioscience, biotechnology, and biochemistry*, 82(8), 1265-1300.
- Betti, C., Della Rovere, F., Piacentini, D., Fattorini, L., Falasca, G., & Altamura, M. M. (2021). Jasmonates, ethylene and brassinosteroids control adventitious and lateral rooting as stress avoidance responses to heavy metals and metalloids. *Biomolecules*, 11(1), 77.
- Veselova, S. V., Nuzhnaya, T. V., Burkhanova, G. F., Rumyantsev, S. D., Khusnutdinova, E. K., & Maksimov, I. V. (2021). Ethylene-cytokinin interaction determines early defense response of wheat against Stagonospora nodorum Berk. *Biomolecules*, 21(13).
- Jaillais, Y., & Chory, J. (2010). Unraveling the paradoxes of plant hormone signaling integration. *Nat. Struct. Mol. Biol.*, 17, 642–645.
- Hluska, T., Hlusková, L., & Emery, R. J. N. (2021). The Hulks and the Deadpools of the cytokinin universe: A dual strategy for Cytokinin Production, Translocation, and Signal Transduction. *Biomolecules*, 11, 209.
- Andrews, S. J., & Rothnagel, J. A. (2014), Emerging evidence for functional peptides encoded by short open reading frames. *Nat. Rev. Genet.*, 15, 193–204.
- Estelle, M. (2011). Auxin Signaling: From Synthesis to Systems Biology; A Subject Collection from Cold Spring Harbor Perspectives in Biology. Cold Spring Harbor, NY: Cold Spring Harbor Laboratory Press.

- Etchells, J. P., Smit, M. E., Gaudinier, A., Williams, C. J., & Brady, S. M. (2016). A brief history of the TDIF-PXY signalling module: balancing meristem identity and differentiation during vascular development. *New Phytol.* 209, 474–484.
- Enders, T. A., & Strader, L. C. (2015). Auxin activity: Past, present, and future. *Am. J. Bot.*, 102, 180–196.
- Blakeslee, J. J., Peer, W. A., & Murphy, A. S. (2005). Auxin transport. *Curr. Opin. Plant Biol.*, 8, 494–500.
- Sun, C. H., Yu, J. Q., Wen, L. Z., Guo, Y. H., Sun, X., Hao, Y. J., Hu, D. G., & Zheng, C. S. (2018). Chrysanthemum MADS-box transcription factor CmANR1 modulates lateral root development via homo-/heterodimerization to influence auxin accumulation in Arabidopsis. *Plant Sci.*, 266, 2.
- Julien, J. D., Pumir, A., & Boudaoud, A. (2019). Strain-or stress-sensing in mechanochemical patterning by the phytohormone auxin. *Bulletin of mathematicalbiology*, 81, 3342-3361.
- Lee, H. W., & Kim, J. (2015). Lateral Organ BoundariesDomain16 and 18 act downstream of the AUXIN1 andLIKE-AUXIN3 auxin influx carriers to control lateralroot development in Arabidopsis. *Plant physiology, 168*, 1792-1806.
- Vlot, A. C., Liu, P. P., Cameron, R. K., Park, S. W., Yang, Y., Kumar, D., ... & Klessig, D. F. (2008). Identification of likely orthologs of tobacco salicylic acid-binding protein 2 and their role in systemic acquired resistance in Arabidopsis thaliana. *The Plant Journal*, 56(3), 445-456.
- Tian, M., von Dahl, C. C., Liu, P. P., Friso, G., van Wijk, K. J., & Klessig, D. F. (2012). The combined use of photoaffinity labeling and surface plasmon resonance-based technology identifies multiple salicylic acid-binding proteins. *The Plant Journal*, 72(6), 1027-1038.
- 17. Dugogi, E. H., Mahdi, N. K., & Matroud, S. A. K. (2012). Response of Indian mustard (Brassica juncea L.) to the distance of planting and spraying with salicylic acid and their effect on growth, seed yield and hard oil. In: Second Scientific Conference of the Faculty of Agriculture, University of Karbala; pp. 173-181.
- Najafian, S., Khoshkhui, M., Tavallali, V., & Saharkhiz, M. J. (2009). Effect of salicylic acid and salinity in thyme (Thymus vulgaris L.): Investigation on changes in gas exchange, water relations, and membrane stabilization and biomass accumulation. *Australian Journal of Basic and Applied Sciences*, 3(3), 2620-2626.
- Raza, S. H., Fahad Shafiq, F. S., Mahwish Chaudhary, M. C., & Imran Khan, I. K. (2013). Seed invigoration with water, ascorbic and salicylic acid stimulates development and biochemical characters of okra (Ablemoschus esculentus) under normal and saline conditions. *International Journal of Agriculture and Biology*, 15, 486-492.

- Sofowora, E. A. (2008). Medicinal plants and traditional medicines in Africa. University of Ife press, Nigeria, pp 1–23.
- Wang, H. (2017). Comparison of phytochemical profiles, antioxidant and cellular antioxidant activities of different varieties of blueberry (Vaccinium spp.). *Food Chem*, 217, 773–781.
- Zakaria, Y., Astal, A. L. (2003). Effect of storage and temperature of aqueous garlic extract on the growth of certain pathogenic bacteria. *J Al Azhar Univ*, 6(2), 11–20.
- Marefati, N., Ghorani, V., Shakeri, F., Boskabady, M., Kianian, F., Rezaee, R., & Boskabady, M. H. (2021). A review of anti-inflammatory, antioxidant, and immunomodulatory effects of Allium cepa and its main constituents. *Pharmaceutical biology*, 59(1), 285-300.
- Chakraborty, A. J., Mitra, S., & Tallei, T. E. (2021). Bromelain a potential bioactive compound: a comprehensive overview from a pharmacological perspective. *Life*, 11(4).
- 25. Mitra, S., Rauf, A., & Tareq, A. M. (2021). Potential health benefits of carotenoid lutein: an updated review. *Food and Chemical Toxicology, 154*.
- El-Demerdash, F., Yousef, M., & El-Naga, N. A. (2005). Biochemical study on the hypoglycemic effects of onion and garlic in alloxan-induced diabetic rats. *Food Chem. Toxicol*, 43, 57–63.
- Campos, K. E., Diniz, Y. S., Cataneo, A. C., Faine, L. A., Alves, M. J., & Novelli, E. L. (2003). Hypoglycaemic and antioxidant effects of onion, Allium cepa: dietary onion addition, antioxidant activity and hypoglycaemic effects on diabetic rats. *Int. J. Food Sci. Nutr, 54*, 241–6.
- Dwivedi, C., & Daspaul, S. (2013). Antidiabetic herbal drugs and polyherbal formulation used for diabetes: A review. J. Phytopharmacol, 2, 44–51.
- 29. Gielen, S., & Landmesser, U. (2014). The Year in Cardiology 2013: cardiovascular disease prevention. *Eur Heart J*, *35*, 307-312.
- Lim, K. H., Ko, D., & Kim, J. H. (2013). Cardioprotective potential of Korean Red Ginseng extract on isoproterenol-induced cardiac injury in rats. *J Ginseng Res*, 37, 273-282.
- Singh, H., Du, J., Singh, P., Mavlonov, G. T., & Yi, T. H. (2018). Development of superparamagnetic iron oxide nanoparticles via direct conjugation with ginsenosides and its in-vitro study. *Journal of Photochemistry and Photobiology B: Biology*, 185, 100-110.
- 32. Dai, L., Liu, K., Si, C., Wang, L., Liu, J., He, J., & Lei, J. (2016). Ginsenoside nanoparticle: a new green drug delivery system. *Journal of materials chemistry B*, 4(3), 529-538.
- 33. Yao, H., Li, J., Song, Y., Zhao, H., Wei, Z., Li, X., Jin, Y., Yang, B., & Jiang, J. (2018). Synthesis of ginsenoside Re-based carbon dots applied for bioimaging and effective inhibition of cancer cells. *Int J Nanomed*, 13, 6249.

- Tunstall-Pedoe, H., Vanuzzo, D., Hobbs, M., Mähönen, M., Cepaitis, Z., Kuulasmaa, K., & Keil, U. (2000). Estimation of contribution of changes in coronary care to improving survival, event rates, and coronary heart disease mortality across the WHO MONICA Project populations. *The Lancet*, 355(9205), 688-700.
- KKAy mice. Arch Pharm Res. 2001;24:214–8. [PubMed] Dey, L., Xie, J. T., Wang, A., Wu, J., Maleckar, S. A., & Yuan, C. S. (2003). Antihyperglycemic effects of ginseng: Comparison between root and berry. *Phytomedicine*, 10, 600–5.
- 36. Etou, H., Sakata, T., Fujimoto, K., Terada, K., Yoshimatsu, H., Ookuma, K., ... & Arichi, S. (1988). Ginsenoside-Rb1 as a suppressor in central modulation of feeding in the rat. *Nihon Yakurigaku Zasshi. Folia Pharmacologica Japonica*, 91(1), 9-15.
- Friedl, R., Moeslinger, T., Kopp, B., & Spieckermann, P. G. (2001). Stimulation of nitric oxide synthesis by the aqueous extract of Panax ginseng root in RAW 264.7 cells. *Br J Pharmacol*, *134*, 1663–70.
- Kim, H. S., Lee, E. H., Ko, S. R., Choi, K. J., Park, J. H., & Im, D. S. (2004). Effects of ginsenosides Rg3 and Rh2 on the proliferation of prostate cancer cells. *Arch Pharm Res*, *27*, 429–35.
- KIMURA, M., WAKI, I., CHUJO, T., KIKUCHI, T., HIYAMA, C., YAMAZAKI, K., & TANAKA, O. (1981). Effects of hypoglycemic components in

ginseng radix on blood insulin level in alloxan diabetic mice and on insulin release from perfused rat pancreas. *Journal of pharmacobio-dynamics*, 4(6), 410-417.

- Kitagawa, I., Yoshikawa, M., Yoshihara, M., Hayashi, T., & Taniyama, T. (1983). Chemical studies on crude drug processing I. On the constituents of Ginseng Radix Rubra. *Yakugaku Zasshi.*, 103, 612–22.
- Dhule, S. S., Penfornis, P., Frazier, T., Walker, R., Feldman, J., Tan, G., He, J., Alb, A., John, V., & Pochampally, R. (2012). Curcumin-loaded γcyclodextrin liposomal nanoparticles as delivery vehicles for osteosarcoma. *Nanomed. Nanotechnol. Biol. Med*, 8, 4.
- Ntoutoume, G. M. N., Granet, R., Mbakidi, J. P., Brégier, F., Léger, D. Y., Fidanzi-Dugas, C., ... & Sol, V. (2016). Development of curcumin– cyclodextrin/cellulose nanocrystals complexes: New anticancer drug delivery systems. *Bioorganic* & medicinal chemistry letters, 26(3), 941-945.
- Guo, S. (2019). Encapsulation of curcumin into βcyclodextrins inclusion: A review. *E3S Web Conf*, *131*, 01100.
- Zhang, L., Man, S., Qiu, H., Liu, Z., Zhang, M., Ma, L., & Gao, W. (2016). Curcumin-cyclodextrin complexes enhanced the anti-cancer effects of curcumin. *Environ. Toxicol. Pharmacol.*, 48, 31–38.