Habtemariam, Med Aromat Plants 2013, 2:4
http://dx.doi.org/10.4172/2167-0412.1000130

Medicinal & Aromatic Plants

Case Report Open Access

The Hidden Treasure in Europe's Garden Plants: Case Examples; *Berberis darwinni* and *Bergenia cordifolia*

Solomon Habtemariam*

Pharmacognosy Research Laboratories, Medway School of Science, University of Greenwich, Chatham-Maritime, Kent ME4 4TB, UK

Abstract

Numerous plants cultivated in European gardens have a history of traditional medicinal uses. Some are native to Europe, while others are introduced from other geographical regions. Systematic pharmacological and phytochemical studies on these plants could yield valuable lead compounds of pharmacological significance. In this short communication, two case examples using *Berberis darwinii* and *Bergenia cordifolia* are presented.

Keywords: European plants; Drug leads; *Berberis darwinii*; *Bergenia cordifolia*

Introduction

For centuries, plants have been used as sources of medicine by mankind. In many developing countries, plant medicines still serve as the primary means of healthcare for treating various illnesses, and current estimates indicate the share of plant-derived drugs in these regions to be about 80% [1]. It is needless to say that Europe and other western countries have recently seen the green medicine resurgence: the ever increasing list of herbal products on the shelves of local pharmacies and health food shops is testimony to people opting to use natural medicines. But how about the secrets within our European garden plants that we might have taken for granted? Some of them have a long history of medicinal uses substantiated by scientific evidence. It is not intended here to list herbal products that are on large scale production for their medicinal uses, but to give two selected examples from common European garden plants that highlight hidden treasures in our gardens.

Traditionally, the search of novel drugs from natural sources take one of the two routs: the ethnobotanical and random screening approach [2]. The ethnobotanical approach starts by documenting the traditional medicinal uses of plants and screen them for biological activities that closely match the indicated disease condition. There are numerous good examples one can use to validate this approach, including the discovery of anticancer drugs, podophyllotoxin derivatives, from studies on *Podophyllum species*. Aremisinin from *Artemisia annua* is another perfect example of the ethnobonatical approach of drug discovery studies. Getting the correct or all information from the ethnobotanical source and even understanding the information, as well as the time scale required for such studies however could be seen as the major challenge of this approach. For those institutions that could afford running hungry assays (e.g. big pharmaceutical industries), the random screening approach using a selected unique target area is an alternative drug discovery approach. This approach, from a well deserved example of the anticancer drug taxol identified from the bark of the Pacific yew tree, *Taxus brevifolia,* has its own success story. When one works in an academic institution like ours where funding is a major constraint, however, a combination of the ethnobotanical and random screening approach study seems very feasible. Hence, we select plants based on ethnobotancal information and use selected high-value targets for pharmacological screening. Whatever strategy is adopted, plants continued to be the source of novel, often structurally complex, chemical entities. Various authors further outlined that about 70% of novel chemicals identified during the last two decades are of natural products origin, of which over half are from plants [1].

Naturally, a drug discovery scientist looks a flora that has not yet been studied and probably those in the tropics and other exotic places with a rich history of traditional uses. There are lots of incentives in studying such plants as the continued deforestation, desertification and over exploitation of endemic plants could lead to their extinction prior to their secret treasures (chemical constituents) being documented. Hence, our research laboratories for over two decades have studied several endemic plants from North and South America, Africa, Asia and Australia. Through systematic pharmacological screening followed by bioassay-guided isolation studies, we have identified various bioactive compounds belonging to several chemical classes [3]. These studies also revealed numerous novel and known chemical entities that could be used for standardization, and/or modernization of traditional herbal medicines. During the course of our study, particularly during the 1990's, we also noticed that there actually exist a big gap in European medicinal plants, with due respect to their chemistry and pharmacology *versus* their claimed medicinal uses. Surprisingly, the chemistry and pharmacology of many European plants, including many acknowledged herbal medicines have not been fully documented. The reasons for these are:

1. There is a general perception that European medicinal plants are exhaustively studied, and there is little chance of getting a pharmacological hit. Most of the earlier studies on European medicinal plants, however, have limitations as the high value targets indentified in recent years were not accounted for. Similarly, our capability today in the isolation and identification of chemical compounds from natural sources is much better than some 50 years ago. Hence, compounds that were difficult to isolate/identify and exist in trace amounts can still be explored from common European plants.

2. It is quite difficult to get funding to document the chemistry and pharmacology of common European plants. European

***Corresponding author:** Dr. Solomon Habtemariam, Pharmacognosy Research Laboratories, Medway School of Science, University of Greenwich, Chatham-Maritime, Kent ME4 4TB, UK, Tel: +44 208 331 8302; Fax: +44 208 331 9805; E-mail: s.habtemariam@gre.ac.uk

Received June 03, 2013; **Accepted** July 22, 2013; **Published** July 25, 2013

Citation: Habtemariam S (2013) The Hidden Treasure in Europe's Garden Plants: Case Examples; *Berberis darwinni* and *Bergenia cordifolia*. Med Aromat Plants 2: 130. doi:10.4172/2167-0412.1000130

pharmacognosists are, therefore, more involved in studying medicinal plants of exotic places than local plants.

In this brief perspective, the chemistry and pharmacology of two selected exemplary European common garden plants (Figure 1) studied in our laboratories during the last two years are presented.

Case Example 1–*Berberis darwinii*

First, let us see an example of botanical treasures discovered by one of the most outstanding British scientists of the 19th century. One might wonder who–perhaps the British chemist Michael Faraday among many other famous scientists of that era; but he was not really known for studying medicinal plants. How about Charles Darwin, whose theory of evolution has drastically shaped science and the human society, as we know it today? Darwin's legendary five-year voyage on H.M.S. Beagle is known to be the foundation for his famous book "*On the Origin of Species*" or the theory of evolution [4]. Besides his widely reported scientific observation in the Galapagos Islands, Darwin meticulously collected exotic plants and animals he encountered during his South American trip. One of the plants that he discovered in 1835, and later named in his honour, was Darwin's Barberry (*Berberis darwinii*). This native plant to southern Chile and Argentina is known to be introduced to Britain in 1849 by *William Lobb* [5]. Darwin's Barberry is now a popular garden and hedging shrub cultivating all over the world. The Royal Horticultural Society has also recently given it an Award of Garden Merit [6]. If one wonders why, this is a fast growing an evergreen plant with dark green shiny leaves and impressive orange flowers in spring that lead to purple-black berries in summer (Figure 1). The mature berries are known to have been eaten by native people in South America for centuries. Apparently, they are acidic and sour, but birds in the Britain greedily feast on them.

Figure 1: Photographs of *Berberis darwinnii* (A) and *Bergenia cordifolia* (B) taken from the author's garden.

Figure 2: Stem wood (A) and steam bark (B) of *B. darwinnii* appearing yellow due to their principal constituent, *Berberine*.

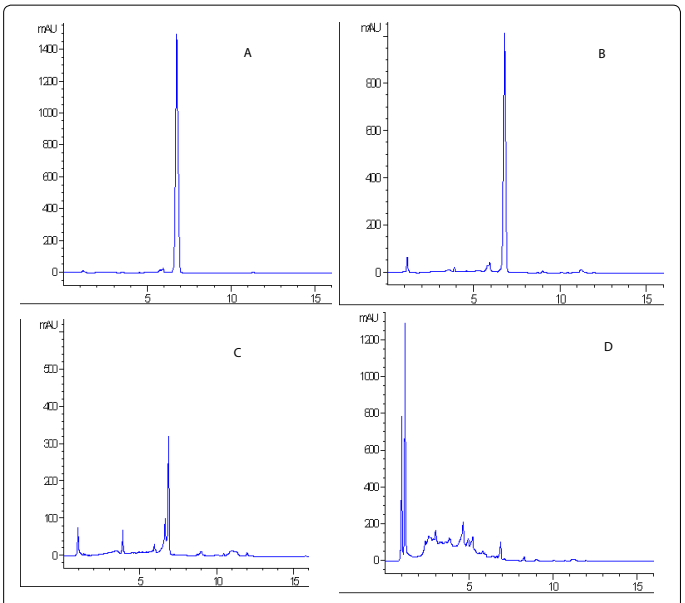

Figure 3: HPLC chromatograms of pure *Berberine* (A), stem bark (B), stem wood (C) and leaves (D) extract of *B. darwinnii*. The extracts were obtained by macerating the plant materials in methanol. HPLC analysis was carried out as described previously [7]. *Berberine* has a retention time of 6.9 min.

If one has to cut the wood of Darwin's Barberry and remove the bark, the woody tissues and bark appear bright yellow in colour (Figure 2); this is due to a chemical called berberine. It is worth noting that plants containing berberine, such as Goldenseal (*Hydrastis canadensis*), and Chinese Goldthread (*Coptis chinensis),* are highly valued for their medicinal uses. But berberine in these plants is found together with other structurally related alkaloids, such as hydrastine, palmatine, and/or jatrorrhizine [7]. We have recently conducted studies on the chemistry and pharmacology of Darwin's Barberry [7]. As shown in Figure 3, HPLC chromatograms revealed the stem bark contained just one UV-visible component, berberine, not just from the alkaloid fraction, but the crude methanolic extract. This finding was remarkable given that plants normally contain a mixture of thousands of different chemicals in their tissues. One of the potential medicinal values of this plant and its chemical berberine that many laboratories looked at so far is for combating Alzheimer's disease (AD).

AD is principally associated with progressive neurodegenerative pathological changes in the forebrain cholinergic system, though other brain areas are also known to be affected. It has been well established that the loss of cholinergic system, and/or decreased levels of acetylcholine is associated with pathological accumulation of β-amyloid protein in the affected areas. One popular therapeutic strategy for AD is, therefore, through enhancing the cholinergic system *via* inhibition of the enzyme (acetylcholinesterase) that breaks down acetylcholine [8]. Agents that reduce the accumulation of β-amyloid or those preventing -amyloid mediated, and/or oxidative-stress associated neurotoxicity could also have beneficial effect in managing AD. Remarkably, Darwin's Barberry extract and its chemical (berberine) have potential to treat AD through the entire above mentioned multiple targets [7]. There is currently a flurry of scientific activities worldwide to synthesize drugs related to this natural product. It is hoped that a more active and easily obtainable anti-AD drug could be found based on this model of natural product. Given that *B. darwinnii* offers a high yield and relatively pure

source of berberine, its potential as anti-AD therapy deserves further investigation.

Berberine has also shown to display numerous other pharmacological properties, including antimicrobial effects against pathogenic bacteria such as *Vibrio cholera, Shigella dysenteriae, Salmonella species* and various multidrug resistant bacterial strains [9-14]. Berberine is widely regarded as a potent anti-inflammatory agent [15-19] that could be explained in part by its action at the molecular level as an inhibitor of leucocytes adhesion to activated endothelial cells [20], cyclooxygenase-2 expression [21,22], NF-κB activation [23], cytokines expression [24], etc. In conjunction with its anti-inflammatory and antioxidant effects, berberine has been shown to display anti-atherosclerosis property [25,26]. The lipid lowering effect of barberine has been reviewed by various authors [27-29], and such effect could partly explain its reputed cardio- and hepatoprotective effects [30,31]. In this connection, the potential of barberine in combating fatty liver diseases has been emphasised in recent years [32-34]. Once again, the protective role of berberine in mammalian tissues could be linked to its antioxidant and anti-inflammatory effects as the expressions of multipotent biomolecules, such as COX-2, proinflammatory cytokines, such as TNF-α and inducible nitric oxide synthase are all inhibited by berberine [35].

The other productive area of research on berberine and berberine-containing plants have been on their potential therapeutic potential for diabetes [36-38], and associated diseases such as diabetic neropathy [39] and nephropathy [40,41]. Among the various possible mechanism of berberine's antidiabetic action are through inhibition of peroxisome proliferator-activated receptors expression [42,43] carbohydrate digestion [44], various signalling pathways [45], modulation of protein tyrosine phosphatase 1B activity [46], activation of glucose transport pathway of GLUT-1 [47], promoting the secretion of glucagon-like peptide secretion [48], increasing insulin receptor expression [49], control of lipid dysregulation [50] antioxidant mechanisms and aldose reductase inhibitory activity [51], and anti-inflammatory mechanisms [52].

Berberine and berberine-containing plants are also highly sought after for their potential anticancer effects. Numerous studies have highlighted that berberine not only directly induces apoptosis in cancer cells [53-55], but also sensitise them to other chemotherapeutic agents and radiation therapy [56,57]. Suppression of gene transcription [58], reactive oxygen species mechanisms [59], mitochondrial and caspase pathways [60], anti-calmodulin property [61] inhibition of key kinase enzymes [62], and many other multiple mechanisms [63] have been suggested as the possible mode of action for berberine-induced apoptosis in cancer cells. Inhibition of cancer metastasis through downregulation of activities and expression levels of key enzymes, such as heparanse [64] and matrix metalloproteinases 2 and 9 [65], are also among the various anticancer study reports on berberine.

In view of the numerous above mentioned exemplary pharmacological activities of berberine, the finding the common garden plant, *B. darwinni,* as a good source of this therapeutically useful drug, is very significant.

Case Example 2–*Bergenia cordifolia*

To date, around 300 million people worldwide are known to suffer from diabetes. Hand in hand with diabetes, obesity has become the most serious public health problem worldwide, and its prevalence during the last few decades has dramatically increased with epidemic proportions [66]. α-Glucosidase and pancreatic lipase enzymes inhibition are two established strategies for targeting diabetes and obesity respectively [67-69]. Other strategies that showed benefit in treating diabetes-related diseases are antioxidant therapeutics [70]. In our laboratories, several hundreds of plants identified from their traditional medicinal uses, and/or scientific reports are screened for digestive enzyme inhibitions and antioxidant effects. Plant extracts that offer multifunctional effects are given priority, and their active constituents subjected to isolation and structural elucidation. One of the promising plants identified in our laboratories was the most widely grown garden plant in Europe, *B. cordifolia.* Though the plant is known to predominantly contain arbutin and bergenin, no comprehensive phytochemical or pharmacological analysis has ever been reported on it.

In addition to potent antioxidant effect, we found that the rhizome extract of *B. cordifolia* was about 103-fold more active in inhibiting α-glucosidase than the standard antidiabetic drug, acarbose [71]. We further demonstrated that this enzyme inhibition by the extract was not a non-selective pharmacological effect as 111-times more potency in α-glucosidase inhibition was observed when compared to mitigation of acetylcholinesterase enzyme activity. By excluding the major constituents (arbutin and bergenin) that do not account both for the antioxidant and potential antidiabetic properties, the search for the minor constituents with the indicated biological activities lead to the identification of three compounds: catechin 3-*O*-gallate, catechin 3,5-di-*O*-gallate and 1,2,4,6-tetra-*O*-galloyl-β-D-glucopyranoside [71]. The latter two compounds were rare natural products isolated as potent natural antilipase [72] and antiviral agents [73], respectively. In addition to displaying the highest level of antioxidant effects, these two compounds further scored 78 and 159-fold respectively more potent α-glucosidase enzyme inhibition than acarbose [71]. Hence, the identified compounds and the plant have enormous therapeutic potential for treating diabetes, obesity and associated diseases.

It is also worth noting the pharmacological activities of the two most abundant *B. cordifolia* constituents; bergenin and arbutin. The most notable biological activity of arbutin is potent inhibition of tyrosinase enzyme that attribuites to its use as a commercial skin lightning agent [74-76]. On the other hand, bergenin has numerous biological effects, including antiviral [77], antiulcer [78], antiarethmetic [79], antidiabetic and anti-obesity [80], anti-inflammatory [81], immunomodulatory [82] and hepatoprotective [83-85] effects.

We have numerous other examples where European garden plants have been shown to display unique pharmacology and chemistry. These plants, as with other plants in exotic places, need to be looked at not only for validating their centuries-old medicinal uses, but also as a source of valuable medicines.

References

1. Habtemariam S (2010) Applying new science for old medicines: Targeting leukocyte-endothelial adhesions by antiiflammatory herbal drugs. Nat Prod Commun 5: 1329-1336.
2. Gyllenhaal C, Kadushin MR, Southavong B, Sydara K, Bouamanivong S, et al. (2012) Ethnobotanical approach versus random approach in the search for new bioactive compounds: support of a hypothesis. Pharm Biol 50: 30-41.
3. http://www.herbalanalysis.co.uk/publications-new.html
4. Darwin C (1859) On the origin of species by means of natural selection, or the preservation of favoured races in the struggle for life. John Murray, London, UK.
5. http://www.brc.ac.uk/plantatlas/index.php?q=node/1297
6. http://www.bbc.co.uk/gardening/plants/plant_finder/plant_pages/88.shtml
7. Habtemariam S (2011) The therapeutic potential of *Berberis darwinii* stem-

bark: quantification of *Berberine* and *in vitro* evidence for Alzheimer's disease therapy. Nat Prod Commun 6: 1089-1090.

8. Khan I, Samad A, Khan AZ, Habtemariam S, Badshah A, et al. (2013) Molecular interactions of 4-acetoxy-plakinamine B with peripheral anionic and catalytic subsites of the aromatic gorge of acetylcholinesterase: Computational and structural insights. Pharm Biol 51: 722-727.
9. Bandyopadhyay S, Patra PH, Mahanti A, Mondal DK, Dandapat P, et al. (2013) Potential antibacterial activity of *Berberine* against multi drug resistant enterovirulent *Escherichia coli* isolated from yaks (*Poephagus grunniens*) with haemorrhagic diarrhoea. Asian Pac J Trop Med 6: 315-319.
10. Kong WJ, Xing XY, Xiao XH, Zhao YL, Wei JH, et al. (2012) Effect of *Berberine* on *Escherichia coli, Bacillus subtilis*, and their mixtures as determined by isothermal microcalorimetry. Appl Microbiol Biotechnol 96: 503-510.
11. Zuo GY, Li Y, Han J, Wang GC, Zhang YL, et al. (2012) Antibacterial and synergy of *Berberine*s with antibacterial agents against clinical multi-drug resistant isolates of methicillin-resistant *Staphylococcus aureus* (MRSA). Molecules 17: 10322–10330.
12. Mekawi M (1966) Effect of *Berberine* alkaloid on *cholera vibro* and its endotoxin. J Egypt Med Assoc 49: 554-559.
13. Fu H, Liu LG, Peng JP, Leng WC, Yang J, et al. (2010) Transcriptional profile of the *Shigella flexneri* response to an alkaloid: *Berberine*. FEMS Microbiol Lett 303: 169-175.
14. Wu LT, Tsou MF, Ho CC, Chuang JY, Kuo HM, et al. (2005) *Berberine* inhibits arylamine N-acetyltransferase activity and gene expression in *Salmonella typhi*. Curr Microbiol 51: 255-261.
15. Fan FL, Dart AM (2012) Anti-inflammatory treatment in patients after percutaneous coronary intervention: Another potential use for *Berberine*? Clin Exp Pharmacol Physiol 39: 404-405.
16. Hong T, Yang Z, Lv CF, Zhang Y (2012) Suppressive effect of *Berberine* on experimental dextran sulfate sodium-induced colitis. Immunopharmacol Immunotoxicol 34: 391-397.
17. Meng S, Wang LS, Huang ZQ, Zhou Q, Sun YG, et al. (2012) *Berberine* ameliorates inflammation in patients with acute coronary syndrome following percutaneous coronary intervention. Clin Exp Pharmacol Physiol 39: 406-411.
18. Wang XH, Jiang SM, Sun QW (2011) Effects of *Berberine* on human rheumatoid arthritis fibroblast-like synoviocytes. Exp Biol Med (Maywood) 236: 859-866.
19. Hu PF, Chen WP, Tang JL, Bao JP, Wu LD (2011) Protective effects of *Berberine* in an experimental rat osteoarthritis model. Phytother Res 201 25: 878–885.
20. Wu YH, Chuang SY, Hong WC, Lai YJ, Chang GJ, et al. (2012) *Berberine* reduces leukocyte adhesion to LPS-stimulated endothelial cells and VCAM-1 expression both *in vivo* and *in vitro*. Int J Immunopathol Pharmacol 25: 741-750.
21. Feng AW, Gao W, Zhou GR, Yu R, Li N, et al. (2012) *Berberine* ameliorates COX-2 expression in rat small intestinal mucosa partially through PPARγ pathway during acute endotoxemia. Int Immunopharmacol 12: 182-188.
22. Feng AW, Yu C, Mao Q, Li N, Li QR, et al. (2011) *Berberine* hydrochloride attenuates cyclooxygenase-2 expression in rat small intestinal mucosa during acute endotoxemia. Fitoterapia 82: 976-982.
23. Huang Z, Meng S, Wang L, Wang Y, Chen T, et al. (2012) Suppression of ox LDL-induced MMP-9 and EMMPRIN expression by *Berberine* via inhibition of NF-κ B activation in human THP-1 macrophages. Anat Rec 295: 78-86.
24. Lin WC, Lin JY (2011) *Berberine* down-regulates the Th1/Th2 cytokine gene expression ratio in mouse primary splenocytes in the absence or presence of lipopolysaccharide in a preventive manner. Int Immunopharmacol 11: 1984-1990.
25. Wu M, Wang J, Liu LT (2010) Advance of studies on anti-atherosclerosis mechanism of *Berberine*. Chin J Integr Med 16: 188-192.
26. Wu M, Wang J (2008) Advance on study in anti-atherosclerosis mechanism of *Berberine*. Zhongguo Zhong Yao Za Zhi 33: 2013–2016.
27. Dong H, Zhao Y, Zhao L, Lu F (2013) The effects of *Berberine* on blood lipids: a systemic review and meta-analysis of randomized controlled trials. Planta Med 79: 437-446.
28. Briand F, Thieblemont Q, Muzotte E, Sulpice T (2013) Up regulating reverse cholesterol transport with cholesteryl ester transfer protein inhibition requires combination with the LDL-lowering drug *Berberine* in dyslipidemic hamsters. Arterioscler Thromb Vasc Biol 33: 13-23.
29. Xiao HB, Sun ZL, Zhang HB, Zhang DS (2012) *Berberine* inhibits dyslipidemia in C57BL/6 mice with lipopolysaccharide induced inflammation. Pharmacol Rep 64: 889-895.
30. Zhao X, Zhang J, Tong N, Chen Y, Luo Y (2012) Protective effects of *Berberine* on doxorubicin-induced hepatotoxicity in mice. Biol Pharm Bull 35: 796-800.
31. Zhu X, Guo X, Mao G, Gao Z, Wang H, et al. (2013) Hepatoprotection of *Berberine* against hydrogen peroxide-induced apoptosis by up regulation of Sirtuin 1. Phytother Res 27: 417-421.
32. Dong H, Lu FE, Zhao L (2012) Chinese herbal medicine in the treatment of non-alcoholic fatty liver disease. Chin J Integr Med 18: 152-160.
33. Yang QH, Hu SP, Zhang YP, Xie WN, Li N, et al. (2011) Effect of *Berberine* on expressions of uncoupling protein-2 mRNA and protein in hepatic tissue of non-alcoholic fatty liver disease in rats. Chin J Integr Med 17: 205-211.
34. Chang X, Yan H, Fei J, Jiang M, Zhu H, et al. (2010) *Berberine* reduces methylation of the MTTP promoter and alleviates fatty liver induced by a high-fat diet in rats. J Lipid Res 51: 2504-2515.
35. Domitrović R, Jakovac H, Blagojević G (2011) Hepatoprotective activity of *Berberine* is mediated by inhibition of TNF-α, COX-2, and iNOS expression in CCl(4)-intoxicated mice. Toxicology 280: 33-43.
36. Chen G, Lu F, Xu L, Dong H, Yi P, et al. (2013) The anti-diabetic effects and pharmacokinetic profiles of *Berberine* in mice treated with Jiao-Tai-Wan and its compatibility. Phytomedicine 20: 780-786.
37. Dong H, Wang N, Zhao L, Lu F (2012) *Berberine* in the treatment of type 2 diabetes mellitus: A systemic review and meta-analysis. Evid Based Complement Alternat Med 2012: 591654.
38. Di Pierro F, Villanova N, Agostini F, Marzocchi R, Soverini V, et al. (2012) Pilot study on the additive effects of *Berberine* and oral type 2 diabetes agents for patients with suboptimal glycemic control. Diabetes Metab Syndr Obes 5: 213-217.
39. Kim SO, Kim HJ (2013) *Berberine* ameliorates cold and mechanical allodynia in a rat model of diabetic neuropathy. J Med Food 16: 511-517.
40. Liu S, Yu N, Zhang XL, Chen XQ, Tang LQ (2012) Regulatory effect of *Berberine* on unbalanced expressions of renal tissue TGF-beta1/SnoN and smad signalling pathway in rats with early diabetic nephropathy. Zhongguo Zhong Yao Za Zhi 37: 3604-3610.
41. Wu D, Wen W, Qi CL, Zhao RX, Lü JH, et al. (2012) Ameliorative effect of *Berberine* on renal damage in rats with diabetes induced by high-fat diet and *Streptozotocin*. Phytomedicine 19: 712-718.
42. Wang M, Wang J, Tan R, Wu Q, Qiu H, et al. (2013) Effect of *Berberine* on PPAR α /NO activation in high glucose- and insulin-induced cardiomyocyte hypertrophy. Evid Based Complement Alternat Med 2013: 285489.
43. Zhou J, Zhou S (2010) *Berberine* regulates peroxisome proliferator-activated receptors and positive transcription elongation factor b expression in diabetic adipocytes. Eur J Pharmacol 649: 390-397.
44. Li ZQ, Zuo DY, Qie XD, Qi H, Zhao MQ, et al. (2012) *Berberine* acutely inhibits the digestion of maltose in the intestine. J Ethnopharmacol 142: 474-480.
45. Xie X, Li W, Lan T, Liu W, Peng J, et al. (2011) *Berberine* ameliorates hyperglycemia in alloxan-induced diabetic C57BL/6 mice through activation of Akt signaling pathway. Endocr J 58: 761-768.
46. Chen C, Zhang Y, Huang C (2010) *Berberine* inhibits PTP1B activity and mimics insulin action. Biochem Biophys Res Commun 397: 543-547.
47. Cok A, Plaisier C, Salie MJ, Oram DS, Chenge J, et al. (2011) *Berberine* acutely activates the glucose transport activity of GLUT1. Biochimie 93: 1187-1192.
48. Lu SS, Yu YL, Zhu HJ, Liu XD, Liu L, et al. (2009) *Berberine* promotes glucagon-like peptide-1 (7-36) amide secretion in streptozotocin-induced diabetic rats. J Endocrinol 200: 159-165.
49. Zhang H, Wei J, Xue R, Wu JD, Zhao W, et al. (2010) *Berberine* lowers blood glucose in type 2 diabetes mellitus patients through increasing insulin receptor expression. Metabolism 59: 285-292.
50. Kim WS, Lee YS, Cha SH, Jeong HW, Choe SS, et al. (2009) *Berberine* improves lipid dysregulation in obesity by controlling central and peripheral AMPK activity. Am J Physiol Endocrinol Metab 296: 812-819.

51. Liu WH, Hei ZQ, Nie H, Tang FT, Huang HQ, et al. (2008) *Berberine* ameliorates renal injury in streptozotocin-induced diabetic rats by suppression of both oxidative stress and aldose reductase. Chin Med J 121: 706-712.

52. Xie W, Du L (2011) Diabetes is an inflammatory disease: Evidence from traditional Chinese medicines. Diabetes Obes Metab 13: 289-301.

53. Xu LN, Lu BN, Hu MM, Xu YW, Han X, et al. (2012) Mechanisms involved in the cytotoxic effects of *Berberine* on human colon cancer HCT-8 cells. Biocell 36: 113-120.

54. He W, Wang B, Zhuang Y, Shao D, Sun K, et al. (2012) *Berberine* inhibits growth and induces G1 arrest and apoptosis in human cholangiocarcinoma QBC939 cells. J Pharmacol Sci 119: 341-348.

55. Park KS, Kim JB, Lee SJ, Bae J (2012) *Berberine*-induced growth inhibition of epithelial ovarian carcinoma cell lines. J Obstet Gynaecol Res 38: 535-540.

56. Wang J, Liu Q, Yang Q (2012) Radio sensitization effects of *Berberine* on human breast cancer cells. Int J Mol Med 30: 1166-1172.

57. Tong N, Zhang J, Chen Y, Li Z, Luo Y, et al. (2012) *Berberine* sensitizes mutliple human cancer cells to the anticancer effects of doxorubicin in vitro. Oncol Lett 3: 1263-1267.

58. Li J, Gu L, Zhang H, Liu T, Tian D, et al. (2013) *Berberine* represses DAXX gene transcription and induces cancer cell apoptosis. Lab Invest 93: 354-364.

59. Li Q, Zhang L, Zu Y, Liu T, Zhang B, et al. (2013) Generation of reactive oxygen species by a novel *Berberine*-bile acid analog mediates apoptosis in hepatocarcinoma SMMC-7721 cells. Biochem Biophys Res Commun 433: 432-437.

60. Yang X, Huang N (2013) *Berberine* induces selective apoptosis through the AMPK-mediated mitochondrial/caspase pathway in hepatocellular carcinoma. Mol Med Rep 8: 505-510.

61. Ma C, Tang K, Liu Q, Zhu R, Cao Z (2013) Calmodulin as a potential target by which *Berberine* induces cell cycle arrest in human hepatoma bel7402 cells. Chem Biol Drug Des 81: 775-783.

62. Park JJ, Seo SM, Kim EJ, Lee YJ, Ko YG, et al. (2012) *Berberine* inhibits human colon cancer cell migration via AMP-activated protein kinase-mediated downregulation of integrin β1 signaling. Biochem Biophys Res Commun 426: 461-467.

63. Chidambara Murthy KN, Jayaprakasha GK, Patil BS (2012) The natural alkaloid *Berberine* targets multiple pathways to induce cell death in cultured human colon cancer cells. Eur J Pharmacol 688: 14-21.

64. Yan L, Yan K, Kun W, Xu L, Ma Q, et al. (2013) *Berberine* inhibits the migration and invasion of T24 bladder cancer cells via reducing the expression of heparanase. Tumour Biol 34: 215-221.

65. Kuo HP, Chuang TC, Tsai SC, Tseng HH, Hsu SC, et al. (2012) *Berberine*, an isoquinoline alkaloid, inhibits the metastatic potential of breast cancer cells via Akt pathway modulation. J Agric Food Chem 60: 9649-9658.

66. http://www.diabetes.co.uk/diabetes-and-obesity.html

67. Habtemariam S (2012) The anti-obesity potential of sigmoidin A. Pharm Biol 50: 1519-1522.

68. Habtemariam S (2013) Antihyperlipidemic components of *Cassia auriculata* aerial parts: Identification through *in vitro* studies. Phytother Res 27: 152-155.

69. Varghese GK, Bose LV, Habtemariam S (2013) Antidiabetic components of *Cassia alata* leaves: Identification through α-glucosidase inhibition studies. Pharm Biol 51: 345-349.

70. Habtemariam S, Cowley RA (2012) Antioxidant and anti-α-glucosidase ccompounds from the rhizome of *Peltiphyllum peltatum* (Torr.) Engl. Phytother Res 26: 1656-1660.

71. Roselli M, Lentini G, Habtemariam S (2012) Phytochemical, antioxidant and anti-alpha-glucosidase activity evaluations of *Bergenia cordifolia*. Phytother Res 26: 908-914.

72. Ivanov SA, Nomura K, Malfanov IL, Sklyar IV, Ptitsyn LR (2011) Isolation of a novel catechin from *Bergenia* rhizomes that has pronounced lipase-inhibiting and antioxidative properties. Fitoterapia 82: 212-218.

73. Duan D, Li Z, Luo H, Zhang W, Chen L, et al. (2004) Antiviral compounds from traditional Chinese medicines *Galla Chinese* as inhibitors of HCV NS3 protease. Bioorg Med Chem Lett 14: 6041-6044.

74. Boissy RE, Visscher M, DeLong MA (2005) Deoxy Arbutin: A novel reversible tyrosinase inhibitor with effective *in vivo* skin lightening potency. Exp Dermatol 14: 601-608.

75. Lin JW, Chiang HM, Lin YC, Wen KC (2008) Natural products with skin-whitening effects. J Food Drug Anal 16: 1-10.

76. Parvez S, Kang M, Chung HS, Bae H (2007) Naturally occurring tyrosinase inhibitors: Mechanism and applications in skin health, cosmetics and agriculture industries. Phytother Res 21: 805-816.

77. Piacente S, Pizza C, DeTommasi N, Mahmood N (1996) Constituents of *Ardisia japonica* and their *in vitro* anti-HIV activity. J Nat Prod 59: 565-569.

78. Abe, K, Sakai K, Uchida M (1980) Effects of *Bergenin* on experimental ulcers-prevention of stress induced ulcers in rats. Gen Pharmacol 11: 361-368.

79. Pu HL, Huang X, Zhao ZH, Hong A (2002) *Bergenin* is the antiarrhythmic principle of *Fluggea virosa.* Planta Med 68: 372-374.

80. Zhang ZY, Lee SY (2003) PTP1B inhibitors as potential therapeutics in the treatment of type 2 diabetes and obesity. Expert Opin Investig Drugs 12: 223-233.

81. Li RW, Leach DN, Myers SP, Lin GD, Leach GJ, et al. (2004) A new anti-inflammatory glucoside from *Ficus racemosa* L. Planta Med 70: 421-426.

82. Nazir N, Koul S, Qurishi MA, Najar MH, Zargar MI (2011) Evaluation of antioxidant and antimicrobial activities of *Bergenin* and its derivatives obtained by chemoenzymatic synthesis. Eur J Med Chem 46: 2415-2420.

83. Lim HK,. Kim HS, Choi HS, Choi J, Kim SH, et al. (2001) Effects of *Bergenin*, the major constituent of *Mallotus japonicus* against d-galactosamine-induced hepatotoxicity in rats. Pharmacol 63: 71-75.

84. Lim HK, Kim HS, Chung MW, Kim YC (2000) Protective effects of *Bergenin,* the major constituent of *Mallotus japonicus*, on D-galactosamine-intoxicated rat hepatocytes. J Ethnopharmacol 70: 69-72.

85. Kim HS, Lim HK, Chung MW, Kim YC (2000) Antihepatotoxic activity of *Bergenin,* the major constituent of *Mallotus japonicas*, on carbon tetrachloride-intoxicated hepatocytes. J Ethnopharmacol 69: 79-83.

Citation: Habtemariam S (2013) The Hidden Treasure in Europe's Garden Plants: Case Examples; *Berberis darwinni* and *Bergenia cordifolia*. Med Aromat Plants 2: 130. doi:10.4172/2167-0412.1000130