Research on plant extracts and phytochemicals: criteria for evaluation

S. Hammad · R. Marchan · H. M. Bolt

Published online: 2 November 2013
© Springer-Verlag Berlin Heidelberg 2013

In the 1990s, the pharmaceutical industry introduced robots that could synthesize thousands of different small molecules in a very short time. Soon, compound libraries with millions of combinatorially produced substances became available. However, despite these impressive numbers, the results were disappointing. Almost all of the produced substances were biologically irrelevant. In addition, the boom in substance research yielded no progress in drug development.

This failure led to a shift in strategy. Many groups subsequently chose to design their compound libraries based on small biologically active molecules found naturally in plants, animals and microorganisms. The obvious advantage of this strategy was the millions of years of evolution that went into optimizing how these natural compounds interact with cells and organisms, for example as messengers or for defence. It is not surprising that many of the currently used drugs, such as taxanes, digitalis, morphine or salicylic acid, have been derived from nature.

Currently, enormous efforts are placed on analysing plant extracts for possible medical applications (Gebhardt 2000; Smith et al. 2013; Katalinic et al. 2006; Wagner 2011; Radojevic et al. 2012; Vasic et al. 2012; Onocha et al. 2011). Examples are hepatotropic (Kheir Eldin et al. 2008; Young et al. 2007; Jain et al. 2012; Eidi et al. 2012; Ikewuchi et al. 2011a, b; Godoy 2011), neurotropic (Qu et al. 2012; van Thriel 2011) and nephrotropic (Venkatanarayana et al. 2012) compounds, as well as antioxidative (Prachayasittikul et al. 2009; Lee et al. 2007; Takashima

et al. 2013; Kędzierska et al. 2013; Abdel-Salam et al. 2012; Çakmak et al. 2012; Naghiloo et al. 2012), antimicrobial (Prachayasittikul et al. 2008; Salleh et al. 2012; Zhu et al. 2011; Darabpour et al. 2011), apoptotic and antiapoptotic (Mishra and Kumar 2009; Ogata et al. 2010; Lu et al. 2009), hypolipidemic (Ansarullah et al. 2009; Amran et al. 2012; Ikewuchi 2012a), antidiabetic (Zardooz et al., 2012; Ikewuchi 2012b), antitumor (Guo and Wang 2009; Khalil et al. 2008; Zeeshan et al. 2012; Tian et al. 2012; Park 2012), anticonvulsant (Bhat et al. 2012a, b), antiarrhythmic (Jahanbakhsh et al. 2012; Esmailidehaj et al. 2012) and anti-inflammatory (Motavallian-Naeini et al. 2012; Kamarudin et al. 2012; Su et al. 2011) substances.

We, at the Archives of Toxicology, receive numerous contributions from scientists whose research focus on the effects of natural compounds. Unfortunately, a relatively high fraction of these manuscripts is rejected by our board of reviewers. This prompted the editors, in the current Editorial, to communicate their criteria for evaluation—which are of course open for comments and discussion. Many of the several hundred studies which were turned down for publication have all used a similar approach. They usually begin by describing how various plant extracts are acquired, without any further characterization of the extracts themselves. Nevertheless, these extracts are added to cells with and without a toxic compound, in an attempt to demonstrate some protective effect. Such studies are usually rejected, because the compounds in the extracts responsible for the protective effect remain unidentified. Therefore, to increase the chance of acceptance, we propose that the submitted studies fulfil the following criteria:

- Bioactive compounds from plant extracts that have been isolated should be identified and their efficiency demonstrated.

S. Hammad · R. Marchan · H. M. Bolt (✉)
Leibniz Institut für Arbeitsforschung an der TU Dortmund,
Leibniz Research Centre for Working Environment and Human
Factors (IfADo), Ardeystrasse 67, 44139 Dortmund, Germany
e-mail: bolt@ifado.de

- Analytical data should be presented which characterize/identify the material that has actually been tested.
- Bioactivity is demonstrated in well-characterized in vitro systems (including positive control compounds) and also in animal models in vivo.
- There are many cases where medical plants may exert therapeutic effects due to interactions with several bioactive compounds. Contributions demonstrating such interactions would be more favourably reviewed.

The editors hope that by outlining their criteria, the decision-making process becomes more transparent to scientists in this important area of research.

References

- Abdel-Salam OME, El Sayed El-Shamarka M, Salem NA, El-Din M, Gaafar A (2012) Effects of *Cannabis sativa* extract on haloperidol-induced catalepsy and oxidative stress in the mice. EXCLI J 11:45–58
- Amran AA, Zakaria Z, Othman F, Das S, Al-Mekhlafi HM, Raj S, Nordin NAMM (2012) Effect of methanolic extract of *Piper sarmentosum* leaves on neointimal foam cell infiltration in rabbits fed with high cholesterol diet. EXCLI J 11:274–283
- Ansarullah TM, Jadeja R, Devkar R, Ramachandran AV (2009) *Oreocnide integrifolia* (Gaud.) MIQ exhibits hypoglycemic and hypolipidemic potentials on streptozotocin diabetic rats: a preliminary dose and duration dependent study. EXCLI J 8:97–106
- Bhat JU, Nizami Q, Asiaf A, Parry SA, Ahmad ST, Aslam M, Khanam R, Mujeeb M, Umar S, Siddiqui A (2012a) Anticonvulsant activity of methanolic and aqueous extracts of *Melissa parviflora* in experimentally induced Swiss albino mice. EXCLI J 11:1–6
- Bhat JU, Parry SA, Aslam M, Ansari S, Nizami Q, Khanam R, Siddiqui A, Ahmad MA (2012b) Anti-seizure activity of flower extracts of *Nepeta bractea* in Swiss albino mice. EXCLI J 11:531–537
- Çakmak YS, Aktumsek A, Duran A (2012) Studies on antioxidant activity, volatile compound and fatty acid composition of different parts of *Glycyrrhiza echinata* L. EXCLI J 11:178–187
- Darabpour E, Poshtkoughian Bavi A, Motamedi H, Seyyed Nejad SM (2011) Antibacterial activity of different parts of *Peganum harmala* L. growing in Iran against multi-drug resistant bacteria. EXCLI J 10:252–263
- Eidi A, Mortazavi P, Bazargan M, Zaringhalam J (2012) Hepatoprotective activity of cinnamon ethanolic extract against CCl₄-induced liver injury in rats. EXCLI J 11:495–507
- Esmailidehaj M, Rasoulian B, Rezvani ME, Delfan B, Mosaddegh-mehrjardi MH, Pourkhalili K (2012) The anti-infarct, antistunning and antiarrhythmic effects of oleuropein in isolated rat heart. EXCLI J 11:150–162
- Gebhardt R (2000) In vitro screening of plant extracts and phytopharmaceuticals: novel approaches for the elucidation of active compounds and their mechanisms. Planta Med 66(2):99–105
- Godoy P (2011) Hepatotoxicity. EXCLI J 10:124–127 (editorial)
- Guo J, Wang M-H (2009) Extract of *Ulmus davidiana* Planch barks induced apoptosis in human hepatoma cell line HepG2. EXCLI J 8:130–137
- Ikwuchi CC (2012a) Hypocholesterolemic effect of an aqueous extract of the leaves of *Sansevieria senegambica* Baker on plasma lipid profile and atherogenic indices of rats fed egg yolk supplemented diet. EXCLI J 11:318–327
- Ikwuchi JC (2012b) Alteration of plasma biochemical, haematological and ocular oxidative indices of alloxan induced diabetic rats by aqueous extract of *Tridax procumbens* Linn (Asteraceae). EXCLI J 11:291–308
- Ikwuchi JC, Uwakwe AA, Onyeike EN, Ikwuchi CC (2011a) Hepatoprotective effect of an aqueous extract of the leaves of *Acalypha wilkesiana* ‘Godseffiana’ Muell Arg (Euphorbiaceae) against carbon tetrachloride induced liver injury in rats. EXCLI J 10:280–289
- Ikwuchi JC, Ikwuchi CC, Igbo NM, Mark-Balm T (2011b) Protective effect of aqueous extract of the rhizomes of *Sansevieria liberica* Gérôme and Labroy on carbon tetrachloride induced hepatotoxicity in rats. EXCLI J 10:312–321
- Jahanbakhsh Z, Rasoulian B, Jafari M, Shekarforoush S, Esmailidehaj M, Mohammadi MT, Aghai H, Salehi M, Khoshbaten A (2012) Protective effect of crocin against reperfusion-induced cardiac arrhythmias in anaesthetized rats. EXCLI J 11:20–29
- Jain M, Kapadia R, Jadeja RN, Thounaojam MC, Devkar RV, Mishra SH (2012) Amelioration of carbon tetrachloride induced hepatotoxicity in rats by standardized *Feronia limonia*. Linn leaf extracts. EXCLI J 11:250–259
- Kamarudin TA, Othman F, Mohd Ramli ES, Md Isa N, Das S (2012) Protective effect of curcumin on experimentally induced arthritic rats: detailed histopathological study of the joints and white blood cell count. EXCLI J 11:226–236
- Katalinic V, Milos M, Kulisic T, Jukic M (2006) Screening of 70 medicinal plant extracts for antioxidant capacity and total phenols. Food Chem 94(4):550–557
- Kędzierska M, Głowacki R, Czernek U, Szydłowska-Pazera K, Potemski P, Piekarski J, Jeziorski A, Olas B (2013) Changes in plasma thiol levels induced by different phases of treatment in breast cancer; the role of commercial extract from black chokeberry. Mol Cell Biochem 372(1–2):47–55
- Khalil WK, Ahmed KA, Park MH, Kim YT, Park HH, Abdel-Wahhab MA (2008) The inhibitory effects of garlic and *Panax ginseng* extract standardized with ginsenoside Rg3 on the genotoxicity, biochemical, and histological changes induced by ethylenediaminetetraacetic acid in male rats. Arch Toxicol 82(3):183–195
- Kheir Eldin AA, Motawi TMK, Sadik NAH (2008) Effect of some natural antioxidants on aflatoxin B1-induced hepatic toxicity. EXCLI J 7:119–131
- Lee HS, Jung SH, Yun BS, Lee KW (2007) Isolation of chebulic acid from *Terminalia chebula* Retz. and its antioxidant effect in isolated rat hepatocytes. Arch Toxicol 81(3):211–218
- Lu MC, Du YC, Chu JJ, Hwang SL, Hsieh PC, Hung CS, Chang FR, Wu YC (2009) Active extracts of wild fruiting bodies of *Antrodia camphorata* (EEAC) induce leukemia HL 60 cells apoptosis partially through histone hypoacetylation and synergistically promote anticancer effect of trichostatin A. Arch Toxicol 83(2):121–129
- Mishra VK, Kumar A (2009) Curcumin induced cell death and inhibition of telomerase activity in mouse lymphoma P388D1 cells. EXCLI J 8:20–29
- Motavallian-Naeini A, Minaian M, Rabbani M, Mahzuni P (2012) Anti-inflammatory effect of ondansetron through 5-HT₃ receptors on TNBS-induced colitis in rat. EXCLI J 11:30–44
- Naghiloo S, Movafeghi A, Delazar A, Nazemiyeh H, Asnaashari S, Dadpour MR (2012) Ontogenetic variation of volatiles and antioxidant activity in leaves of *Astragalus compactus* Lam. (Fabaceae). EXCLI J 11:436–443
- Ogata I, Kawanai T, Hashimoto E, Nishimura Y, Oyama Y, Seo H (2010) Bisabololoxide A, one of the main constituents in German chamomile extract, induces apoptosis in rat thymocytes. Arch Toxicol 84(1):45–52
- Onocha PA, Oleyede GK, Afolabi QO (2011) Phytochemical investigation, cytotoxicity and free radical scavenging activities of

- non-polar fractions of *Acalypha hispida* (leaves and twigs). EXCLI J 10:1–8
- Park SU (2012) Anticancer compounds from plants. EXCLI J 11:386–389 (editorial)
- Prachayasittikul S, Suksrichavalit T, Isarankura-Na-Ayudhya C, Ruchirawat S, Prachayasittikul V (2008) Antimicrobial and antioxidative activities of 1-adamantylthio derivatives of 3-substituted pyridines. EXCLI J 7:63–70
- Prachayasittikul S, Worachartcheewan A, Lawung R, Ruchirawat S, Prachayasittikul V (2009) Activities of thiotetrahydropyridines as antioxidant and antimicrobial agents. EXCLI J 8:107–114
- Qu ZQ, Zhou Y, Zeng YS, Lin YK, Li Y, Zhong ZQ, Chan WY (2012) Protective effects of a *Rhodiola crenulata* extract and salidroside on hippocampal neurogenesis against streptozotocin-induced neural injury in the rat. PLoS ONE 7(1):29641
- Radojević ID, Stanković MS, Stefanović OD, Topuzović MD, Čomić LR, Ostojić AM (2012) Great horsetail (*Equisetum telmateia* Ehrh.): active substances content and biological effects. EXCLI J 11:59–67
- Salleh WM, Ahmad F, Sirat HM, Yen KH (2012) Chemical compositions and antibacterial activity of the leaf and stem oils of *Piper porphyrophyllum* (Lindl.) N.E. Br. EXCLI J 11:399–406
- Smith MJ, Germolec DR, Frawley RP, White KL Jr (2013) Immunomodulatory effects of black cohosh (*Actaea racemosa*) extract in female B6C3F1/N mice. Toxicology 308:146–157
- Su J-Y, Li Q-C, Zhu L (2011) Evaluation of the in vivo anti-inflammatory activity of a flavone glycoside from *Cancrinia discoidea* (Ledeb.) Poljak. EXCLI J 10:110–116
- Takashima M, Nara K, Niki E, Yoshida Y, Hagihara Y, Stowe M, Horie M (2013) Evaluation of biological activities of a groundnut (*Apios americana* Medik) extract containing a novel isoflavone. Food Chem 138(1):298–305
- Tian Q, Cui H, Li Y, Lu H (2012) LY294002 induces differentiation and inhibits invasion of glioblastoma cells by targeting GSK-3 β and MMP. EXCLI J 11:68–77
- van Thriel C (2011) Recent research in neurotoxicology. EXCLI J 10:135–137
- Vasić SM, Stefanović OD, Ličina BZ, Radojević ID, Čomić LR (2012) Biological activities of extracts from cultivated *Granadilla Passiflora alata*. EXCLI J 11:208–218
- Venkatanarayana G, Sudhakara G, Sivajyothi P, Indira P (2012) Protective effects of curcumin and vitamin E on carbon tetrachloride-induced nephrotoxicity in rats. EXCLI J 11:641–650
- Wagner H (2011) Synergy research: approaching a new generation of phytopharmaceuticals. Fitoterapia 82(1):34–37
- Young SC, Wang CJ, Lin JJ, Peng PL, Hsu JL, Chou FP (2007) Protection effect of piper betel leaf extract against carbon tetrachloride-induced liver fibrosis in rats. Arch Toxicol 81(1):45–55
- Zardooz H, Zahediasl S, Rostamkhani F, Farrokhi B, Nasiraei S, Kazeminezhad B, Gholampour R (2012) Effects of acute and chronic psychological stress on isolated islets' insulin release. EXCLI J 11:163–175
- Zeeshan M, Rizvi SMD, Khan MS, Kumar A (2012) Isolation, partial purification and evaluation of bioactive compounds from leaves of *Ageratum houstonianum*. EXCLI Journal 11:78–88
- Zhu L, Tian Y-J, Yang L, Jiang J-G (2011) Chemical composition and antimicrobial activities of essential oil of *Blumea megacephala*. EXCLI J 10:62–68