Toxicity Studies

In this guide

In vitro and in vivo studies

Acute toxicity

E. purpurea

30. No adverse effects were observed when expressed juice from E. purpurea was administered either orally or intravenously to 8 week old Wistar rats and NMRI mice following Good Laboratory Practice (GLP) and the OECD recommendations for technical methods at the time of the study (Mengs et al., 1991). Eight animals of each sex were given a single oral dose via gastric tube 15,000 mg/kg bw in rats and 30,000 mg/kg bw in mice. The intravenous dose was administered to eight animals of each sex via the tail vein at 5,000 mg/kg bw in rats and 10,000 mg/kg bw in mice. The animals were observed for 14 days and

inspected several times daily and at the end of the experiment a necropsy with macroscopic inspection was performed. There were no deaths or any signs of abnormalities or toxicity due to the Echinacea. The authors concluded that a lethal dose cannot be found and LD50 was not calculated.

E. angustifolia

31. An acute toxicity study was performed with E. angustifolia following the OECD-423 criteria (Espinosa-Paredes et al., 2021). Briefly, three CD-1 male mice received a single dose of 2,000 mg/kg bw of the ethyl acetate extract and were monitored for 14 days for clinical signs and mortality. No adverse effects such as piloerection, mucosal irritation, altered motor activity, or death were observed. Necropsy revealed no macroscopic lesions in major organs, including lungs, kidneys, heart, stomach, intestines, spleen, and liver. Based on these findings, the authors classified the LD50 of the ethyl acetate extract as Category 5 under the Globally Harmonized System (GHS) (>2,000–5,000 mg/kg), indicating very low acute toxicity and potential risk only for vulnerable populations.

Subacute toxicity

E. purpurea

32. Expressed juice from E. purpurea was administered via oral gavage to groups of 18 Wistar rats per sex at doses of 0, 800, 2,400, or 8,000 mg/kg body weight daily for four weeks (Mengs et al., 1991). A statistically significant reduction in plasma alkaline phosphatase was observed in males at 2,400 and 8,000 mg/kg, while females exhibited a significant increase in prothrombin time at the same dose levels compared to controls. The authors concluded that since the alkaline phosphatase and prothrombin time were still in the normal physiological variation range for the rat strain used and there was no dose dependent response, no toxicological point of departure could be derived from the data. The study noted that all other parameters, including biochemical and haematological results, body weight, food consumption, ophthalmological findings, necropsy, and histopathology, showed no significant differences among treatment groups.

E. angustifolia

33. Espinosa-Paredes et al. (2021) conducted a 28-day repeated-dose toxicity study with ethyl acetate extract of E. angustifolia. The extract was administered

to five CD-1 mice per dose per sex at 20 mg/kg bw or 200 mg/kg bw. Serum aspartate aminotransferase (AST), alanine aminotransferase (ALT) and creatinine levels were determined. No statistically significant differences were observed between treated and control groups, and the authors concluded that there was no evidence of liver or kidney toxicity associated with Echinacea extract administration.

Sub-chronic toxicity

34. The toxicity of E. purpurea extract was evaluated in a 13-week repeated oral dose toxicity test in Sprague Dawley rats (Jeong et al., 2024). The study was conducted in compliance with GLP regulations and the Korean Food and Drug Administration's Test Guidelines for Toxicity Studies of Drugs. The E. purpurea extract, standardised to contain at least 2% chicoric acid, was administered daily at doses of 0, 500, 1,000, and 2,000 mg/kg body weight to groups of 10 rats per sex. No mortality or abnormal clinical signs were observed in either sex at any of the tested doses. Ophthalmological examinations, absolute and relative organ weights, haematology, and serum biochemistry showed no significant differences between treated and control groups. The urinalysis revealed a statistically significant increase in mean urine volume in males at 1,000 mg/kg compared to controls. Some individual variations were also observed in the urinalysis, but they were not significantly different when compared to the controls.

Cytotoxicity

35. Tsai et al. (2012a) investigated the cytotoxicity of E. purpurea flower extract and its bioactive constituent chicoric acid in human colorectal cancer cell lines (HCT-116 and Caco-2). Treatment with Echinacea extract (0–2,000 µg/mL) for 24 hours did not affect cell viability, but a dose-dependent reduction was observed at 48 hours. Chicoric acid significantly decreased cell viability at ≥150 µg/mL after 24 hours and at all tested concentrations (50–200 µg/mL) after 48 hours. In HCT-116 cells, chicoric acid (50–150 µg/mL) suppressed telomerase activity, induced DNA fragmentation, activated caspase-9, and promoted PARP cleavage, indicating apoptosis. The authors concluded that the possible in vitro cytotoxicity mechanism of E. purpurea extract is mediated by repression of telomerase activity, activation of caspase pathway and induction of apoptosis.

Genotoxicity

E. purpurea

36. No genotoxic effects were observed in an in vitro bacterial reverse mutation assay, a mouse lymphoma assay, human lymphocyte assay and a micronucleus test performed by Mengs et al. (1991) using lyophilised E. purpurea expressed juice from the commercial product Echinacin Liquidum. The GLP OECD guidelines and the OECD recommendations for technical methods at the time of the study were followed. Details of the Mengs et al. (1991) tests and the authors conclusions are provided below.

37. The bacterial reverse mutation test evaluated lyophilised E. purpurea expressed juice at 8–5,000 µg/plate in S. typhimurium strains TA98, TA100, TA1535, TA1537, TA1538, with and without S9 metabolic activation. No dose-related or statistically significant increase in revertant colonies was observed, indicating no mutagenic activity.

38. The mouse lymphoma assay involved testing lyophilised E. purpurea expressed juice concentrations of 50–5,000 µg/mL in L5178Y mouse lymphoma cells, with and without S9 metabolic activation. No significant increase in mutation frequency was detected at any concentration, and the test material was virtually non-toxic up to 5,000 µg/mL.

39. For the in vitro chromosomal aberration test, the lyophilised Echinacin Liquidum was tested at 2,400–5,000 µg/mL in human lymphocyte cultures, with and without S9 metabolic activation. There was no evidence of mitotic inhibition following the Echinacea treatment of up to 5,000 µg/mL A small, but statistically significant increase in the proportion of cells with structural aberrations was observed at 5,000 µg/mL at the 20 h sampling point in the absence of S9, but it was considered biologically insignificant by the authors as it well within the range of biological control.

40. The in vivo micronucleus test involved the administration of Echinacin Liquidum orally at 25,000 mg/kg to 5 male and 5 female mice. Bone marrow analysis at 24, 48, and 72 h post-dose showed no significant increase in micronucleated polychromatic erythrocytes compared to controls.

41. An in vitro cell transformation assay was performed using lyophilised E. purpurea extract using Syrian hamster embryo cells (SHE) (Mengs et al., 1991). Six concentrations (5–55 µg/mL) were tested in two independent experiments (20 replicates per concentration), with benzo(a)pyrene as a positive control. After 7 days of incubation, colonies were evaluated for morphological transformation. The study reported no significant difference in the frequencies of morphologically transformed colonies between the treatment groups and the negative control,

and the authors concluded that there was no evidence of malignant transformation induced by Echinacea extract.

42. The mutagenicity and the antimutagenic effects of E. purpurea were tested in S. typhimurium TA 98 and TA 100 strains with and without S9 metabolic activation at a maximum concentration of 5 mg/plate (Tsai et al., 2012b). The E. purpurea extracts showed no toxicity against S. typhimurium strains TA98 and TA100 concentrations of ≤5.0 mg/plate, with or without S9 metabolic activation (Tsai et al., 2012b). None of the tested concentrations of E. purpurea showed any significant differences in the revertant number with or without S9 mix. The Echinacea extract however showed a dose-dependent inhibitory effect on the mutagenicity of 2-aminoanthracene in both S. typhimurium strains.

43. Jeong et al. (2024) assessed the genotoxic potential of E. purpurea extract using three assays: an in vitro bacterial reverse mutation test (OECD 471), an in vitro chromosomal aberration test (OECD 473), and an in vivo micronucleus test (OECD 474). For the bacterial reverse mutation assay, the extract was tested up to 5,000 µg/plate in S. typhimurium strains TA98, TA100, TA1535, TA1537 and E. coli WP2uvrA, with and without S9 activation. No growth inhibition or increase in revertant colonies was observed at any dose and results were considered negative for mutagenicity. For the in vitro chromosomal aberration test, Chinese Hamster Lung (CHL/IU) cells were treated with up to 313 µg/mL extract, with or without metabolic activation. No statistically significant increase in structural or numerical chromosomal aberrations was observed compared to controls. In the in vivo micronucleus test, seven-week-old male Sprague Dawley rats received E. purpurea extract at 1,250–5,000 mg/kg bw (two doses; 5 animals per dose). Bone marrow analysis showed no statistically significant increase in micronucleated polychromatic erythrocytes compared to negative controls. Based on these findings, the authors concluded that no evidence of genotoxicity was observed across all three assays.

E. angustifolia

44. The mutagenicity of E. angustifolia was tested using an in vitro bacterial reverse mutation test in S. typhimurium TA98, TA100 and TA102 in the presence and absence of S9 metabolic activation mix (Espinosa-Paredes et al., 2021). A test was considered positive when the number of spontaneous colonies exceeded twice the number of basal revertants. The authors reported that the tested concentrations of E. angustifolia extract, with or without S9 mix, did not yield a positive test and no genotoxic activity was therefore observed.

45. Espinosa-Paredes et al. (2021) conducted an in vivo micronucleus test in male CD-1 mice to assess genotoxicity of an ethyl acetate extract of E. angustifolia administered intragastrically at 1,000 mg/kg bw to three animals. The frequencies of normochromatic erythrocytes (NCEs) and reticulocytes (RETs), with and without micronuclei (MNs), were evaluated in order to calculate the percentages of mature normochromatic erythrocytes (% MN-NCEs), micronucleated reticulocytes (% MN-RETs) and total reticulocytes (% RETs). The E. angustifolia extract did not induce a significant increase in micronuclei formation, with %MN-RET at 0.9% compared to 0.3% in the negative control. A decrease in the frequency of RET in the Echinacea extract group compared with the negative control (2.56% vs 5.41%, $p < 0.05$) was reported, but the authors did not comment on its biological relevance.

Reproductive and developmental effects of Echinacea

46. There are limited data from animal and human studies on the reproductive and developmental effects of Echinacea and its subsequent safety during pregnancy and lactation. The stages of the reproductive and developmental cycle covered by the available animal and human studies on the effects of Echinacea during the reproductive and developmental period are outlined in Table 1. Further information on the reproductive and developmental cycle stages and the scope of the maternal diet papers can be found in Scope of the Nutrition and maternal health project Annex (TOX/2025/44).

Table 1: Reproductive and developmental cycle stages covered by available Echinacea animal and human studies.

Study reference	Study type	*Echinacea* preparation and dose	Stage A (pre-mating to conception)	Stage B (conception to implantation)	Stage C (implantation to closure of hard palate)	Stage D (closure hard palate end of pregna

Chow *et al*. 2006	Animal study (DBA/2 mice)	*E. purpurea* extract 0.45 mg/kg bw/day (dose per body weight)	Not covered	Covered	Covered	Covered
Barcz *et al*. 2007	Animal study (Balb/c mice)	*E. purpurea* extract 0.6 mg/day	Not covered	Covered	Covered	Covered
Khaksary Mahabady *et al*., 2006	Animal study (NMRI mice)	*E. purpurea* extract 360 mg/kg	Not covered	Covered	Covered	Covered
Maass et al., 2005)	Animal study (pigs)	*E. purpurea* dried cobs 0.5-3.6%	Not covered	Not covered	Not covered	Covered
Dabbou *et al*., 2016	Animal study (rabbits)	*E. pallida* 3 g/kg	Not covered	Covered	Covered	Covered
Kovitvadhi *et al*., 2016	Animal study (rabbits)	*E. pallida* 3 g/kg	Not covered	Not covered	Not covered	Not cov
Gallo *et al*., 2000	Human prospective controlled study	*E. purpurea* and *E. angustifolia* 250- 1000 mg/day	Unknown	Covered	Covered	Covered

Heitmann *et al*., 2016	Human prospective cohort study	Not known	Unknown	Covered	Covered	Covered
Cuzzolin *et al*., 2010	Human cross-sectional study	Not known	Unknown	Unknown	Unknown	Unknow
Nordeng *et al*., 2011	Human cross-sectional study	Not known	Unknown	Unknown	Unknown	Unknow
Matthias *et al*., 2008	Human case report	Four tablets each containing *E. purpurea* 675 mg and *E. angustifolia* 600 mg	Not covered	Not covered	Not covered	Not cov

*See Annex Scope of the Nutrition and maternal health (TOX/2025/44) for further information on reproductive and developmental cycle.

47. There are no guidelines conforming in vivo studies on the reproductive and developmental toxicity of medicinally used Echinacea species. There are several studies investigating the effects of E. purpurea during pregnancy in mice (Barcz, E. et al., Chow et al., 2006) and pigs (Maass et al., 2005). The reproductive and immune parameters of E. pallida were investigated in pregnant rabbits (Dabbou et al., 2016) and their offspring (Kovitvadhi et al., 2016). No studies were found on the reproductive effects of E. angustifolia. The animal studies describing the reproductive and developmental effects of Echinacea are outlined below.

E. purpurea

48. Chow et al. (2006) investigated the potential association between E. purpurea consumption and spontaneous abortion in pregnant DBA/2 mice. Six mice were fed Echinacea-supplemented chow from conception and sacrificed at either gestational days 10–11 (early pregnancy) or 12–14 (mid pregnancy). Commercially prepared E. purpurea extract was homogenized into finely ground standard chow that individual mice consumed Echinacea at 0.45 mg/kg bw/day. Echinacea-fed mice showed reduced spleen lymphocytes and nucleated erythroid cells, aligning with levels in non-pregnant mice. The bone marrow parameters were not influenced by the Echinacea supplementation. Although early pregnancy (days 10–11) showed no significant difference in foetal count, by days 12–14, only 50% of foetuses survived in the Echinacea group compared to controls (4.0/pregnancy in controls vs 2.0/pregnancy in treatment group). The authors concluded that Echinacea may increase miscarriage risk in early pregnancy and advised against its use during this period.

49. Barcz et al. (2007) investigated the effects of Echinacea on the angiogenic activity and tissue vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF) in foetuses from pregnant Balb/c mice exposed to E. purpurea extracts. Eight mice received 0.6 mg of Echinacea extract daily from fertilisation to gestation day 18 (three Esberitox, two Immunal, three Echinapur). On day 18, foetuses were collected, pooled, and analysed. Echinapur and Esberitox groups showed a non-significant reduction in mean litter size compared to controls. However, all Echinacea treatments significantly reduced foetal VEGF and bFGF levels ($p < 0.0001$). Angiogenic activity increased significantly in the Esberitox group, decreased in the Immunal group, and remained unchanged with Echinapur. The study concluded that E. purpurea preparations may influence foetal angiogenesis and should not be recommended in pregnancy without further studies being carried out.

50. Khaksary Mahabady et al. (2006) assessed whether E. purpurea extract or levamisole could reduce phenytoin-induced cleft palate in NMRI mice. Thirty-two pregnant NMRI mice were divided into four groups: saline control (10 mL/kg), phenytoin only (65 mg/kg), phenytoin (65 mg/kg) + levamisole (10 mg/kg), and phenytoin (65 mg/kg) + E. purpurea extract (360 mg/kg). All drugs were administered intraperitoneally from the first day of gestation, which was assumed to be upon the discovery of vaginal plug following mating. The study reported that phenytoin alone caused cleft palate in 16% of foetuses, while levamisole and E. purpurea reduced this to 5.3% and 3.2%, respectively. Foetal weight and

length were significantly reduced in the phenytoin group but remained normal in the treatment groups. The authors concluded that the observed protective activity of levamisole and Echinacea against phenytoin-induced cleft palate was due to immunomodulating and anti-inflammatory effects of these agents.

51. Maass et al. (2005) evaluated the effects of dietary E. purpurea in pregnant sows from day 85 of gestation to day 28 of lactation. Thirty-six sows were divided into three groups receiving 0%, 1.2%/0.5%, or 3.6%/1.5% Echinacea during pregnancy/lactation. No adverse effects were observed in sows or piglets. While sows in the control group gained more weight during gestation, no significant differences were found in lactation weight loss, piglet birth weight, or growth performance. The study concluded that Echinacea supplementation had no significant impact on sow or piglet health.

E. pallida

52. Two linked studies investigated the effects of E. pallida supplementation in rabbits. In the first study (Dabbou et al., 2016), 100 pregnant does were fed either a standard diet or one supplemented with 3 g/kg E. pallida from insemination to weaning. The Echinacea preparation contained caftaric acid, chicoric acid, chlorogenic acid and echinacoside with echinacoside found to be the main caffeic acid derivative. The study concluded that supplementation with E. pallida did not show any significant effects on the reproductive, haematological, or immune parameters of does.

53. The second study (Kovitvadhi et al., 2016) assessed the offspring of these does. Eighty weaned kits were allocated into four groups based on maternal diet and post-weaning diet: (1) offspring from control does fed the control diet, (2) offspring from control does fed the supplemented diet, (3) offspring from Echinacea-supplemented does fed the control diet, and (4) offspring from Echinacea-supplemented does fed the supplemented diet. The diets consisted of a commercial basal feed with or without E. pallida supplementation (3 g/kg). Parameters measured included growth, microbiome composition, blood biochemistry, phagocytic activity, and humoral immune response. While phagocytosis increased in supplemented groups, no significant differences were found in other outcomes. The study concluded that there were no significant differences in growth performances, blood parameters, bacterial community, or humoral immune response in the offspring.

Human studies

54. A systematic review conducted on the available literature up to 2006 (Perri et al., 2006) concluded that good scientific evidence from a prospective follow up study (Gallo et al., 2000) showed that oral consumption of Echinacea during the first trimester did not increase the risk of major malformations. Perri et al (2006) noted that The German Commission E compendium produced by an expert panel on a botanical medicine (Blumenthal et al., 1998) had concluded that Echinacea was not teratogenic and oral consumption of Echinacea in recommended doses was safe during pregnancy and lactation. However, the expert panel had advised that caution should be exercised until there was stronger evidence on the safety of Echinacea during lactation.

55. A prospective controlled study by Gallo et al. (2000) involving 206 pregnant women, enrolled and prospectively followed up after contacting the Motherisk Program, assessed the safety of Echinacea use during pregnancy. Participants were matched with controls for age, alcohol use, and smoking. In this study group, 112 women (54%) used Echinacea in the first trimester, with 17 (8%) exposed in all 3 trimesters. A total of 114 (58%) of 198 respondents used capsule or tablet preparations, or both, of Echinacea (250 to 1000 mg/d); 76 (38%) of the subjects used tinctures (5 to 30 drops per day). The self-reported duration of use was between 5 and 7 days. Different brands of E. purpurea and E. angustifolia were used, but the number of women using each species was not specified; E. pallida was only used by one woman. The study reported no significant differences between Echinacea users and controls in terms of pregnancy outcomes, including birth weight, gestational age, or malformation rates. Among Echinacea users

Echinacea use during organogenesis did not increase the risk of major malformations.

56. The Norwegian Mother and Child Cohort Study (Heitmann et al., 2016) investigated Echinacea use during pregnancy among 363 women (0.5% of participants) as part of a prospective population-based pregnancy cohort study. The most common reasons for Echinacea use were treatment of cold/flu, upper respiratory tract infections (including sinusitis, otitis, tonsillitis, and cough), lower respiratory tract infections (bronchitis and pneumonia), vaginal and oral herpes infections. Echinacea supplements were taken during early (206 women) and late (183 women) pregnancy, though timing details were incomplete, and dosage/preparation were unspecified. No increased risks were found for preterm birth, low birth weight, or small for gestational age. No increased risk of

malformations was detected amongst the women who had used Echinacea during early pregnancy compared to controls; adjusted OR (95% CI) = 1.1 (0.6–2.1). There was 1.5% prevalence of major malformations in the women who had used Echinacea compared with 2.6%

57. In a 10-month study at maternity wards in Padua and Rovereto, Italy, using structured anonymous questionnaire, 27.8% of 392 women reported using herbal remedies during pregnancy (Cuzzolin et al., 2010). Echinacea was used orally by 10 women (9.2%) for colds, anxiety, and immune support. Details on species, dosage, and timing were not specified. By examining each herb separately, the authors reported that in one case there was a possible relationship between prolonged Echinacea intake and intrauterine growth restriction in a 35-week newborn. No further details were provided for that case.

58. A similar study aiming to investigate the use of herbal medicines in pregnant women in relation to pregnancy outcomes involved the administration of a structured questionnaire to 600 women within five days after delivery at Stavanger University Hospital Norway (Nordeng et al., 2011). 40% of women reported to have used herbal medicines during pregnancy, with Echinacea being used by 45 (7.5%) of those interviewed for cold and flu symptoms. No details were provided on Echinacea species, dosage, or timing. Birthweights were significantly higher among herbal users (mean 3,663 g vs. 3,508 g; p = 0.001), attributed to iron-rich herbs. No specific association between Echinacea use and birthweight or other outcomes was discussed.

Lactation

59. A case study examined the bioavailability of Echinacea alkylamides in human breast milk in a 35 year old volunteer at six different time points after ingestion of four Echinacea Premium tablets (Matthias et al., 2008). The tablets were prepared from dried ethanolic extracts of two Echinacea species and each tablet contained the equivalent of 675 mg E. purpurea root and 600 mg E. angustifolia root. A total of 13.1 mg of N-isobutyldodeca-2E,4E,8Z,10E/Z-tetraenamide alkylamides were ingested by the volunteer and they were found in the breast milk between 1 and 4 hours after the administration of the Echinacea tablets. Further details were not present in this conference abstract.

Adverse effects in humans

60. A meta-analysis of clinical trials (Schapowal et al., 2015) investigating the use of Echinacea in patients with respiratory tract infections looked at the adverse events recorded in the 6 clinical trials included in the analysis from a total of 1,440 Echinacea-treated subjects and 1,326 subjects receiving placebo. The studies used varying Echinacea preparations and doses. Four studies employed ethanol/glycerol extractions from E. purpurea/E. angustifolia (500–4,000 mg extract/day), and two used pressed juices from E. purpurea (6,200–10,000 mg/day). Overall, 491 adverse events occurred with Echinacea in comparison to 474 with placebo, but there were no significant differences between the groups. Most adverse effects reported were gastrointestinal disturbances and were mild and transient. Only two severe adverse events (stridor) occurred with Echinacea and one (glandular fever, requiring hospitalisation) in the placebo group. There were no significant differences in clinical biochemistry associated with Ec

61. The EMA assessment report on E. purpurea (EMA, 2014) concluded that based on the analysis of pharmacovigilance reports from EU member states, hypersensitivity reactions such as rash, urticaria, itching and swelling were possible adverse effects of Echinacea and in a case of allergic reaction, Echinacea should not be taken again. The EMA report stated that there were cases of severe reactions such as Stevens-Johnson Syndrome, angioedema, bronchospasm, asthma and anaphylactic shock with confirmed/probable causality. The report acknowledged that cases of autoimmune diseases such as encephalitis disseminata, erythema nodosum, immunothrombocytopenia, Sjögren’s syndrome with renal tubular dysfunction were reported, but that their causality was inconclusive. The report further stated that gastrointestinal side effects reported were unlikely to be linked to Echinacea as their frequency was similar between the placebo and treatment groups in clinical trials (EMA, 2014).

62. A systematic review summarised evidence of the safety of Echinacea based herbal medicinal products from 36 clinical studies, case reports, and spontaneous reporting programmes from regulatory agencies in Australia, Germany, UK, USA and Sweden (Huntley et al., 2005). The oral doses used in the clinical trials were typically 4-8 mL expressed juice/liquid extract twice daily, 250-1,000 mg daily in the form of capsules/tablets or 5-30 drops daily for the tinctures. The review concluded that Echinacea had a good safety profile when taken short-term, with short-term use being defined as ‘days as opposed to weeks’. Adverse effects were mild, transient and reversible with gastrointestinal disturbances and skin-related reactions being most commonly reported. The review discussed that in rare cases Echinacea use can be associated with allergic

reactions, which can be severe. However, the authors noted that in about a quarter of these cases, Echinacin ® (E. purpurea) was administered intramuscularly or intravenousl

63. An Australian study looking at adverse reactions associated with Echinacea reviewed 51 reports of adverse drug reactions (ADRs)in the Australian Adverse Drug Reactions Advisory Committee's database (Mullins and Heddle, 2002). There were 26 cases which were suggestive of IgE-mediated hypersensitivity reactions (4 anaphylaxis, 12 acute asthma,10 urticaria/angioedema). Seventy eight percent of the affected patients were female, median age was 32 years and over half had a history of asthma, allergic rhinitis or atopic dermatitis. In addition to the review of the ADR reports, five cases of adverse reactions to Echinacea were personally evaluated by the authors. Two patients suffered anaphylaxis and a third had an acute asthma attack 10 minutes after their first ever dose of Echinacea. All three patients were female, had a history of atopy including allergic rhinitis or latex allergy and tested positive on skin prick tests to aqueous Echinacea. A fourth case described a 56-year-old man who developed recurrent

64. There are individual case reports of adverse effects experienced by people after taking Echinacea preparations including an autoimmune disease supposedly triggered by Echinacea (Lee and Werth, 2004), isolated case of erythema nodosum in a 41-year old male (Lee Soon and Crawford, 2001), hypereosinophilia in a 58-year old male patient with history of asthma and allergic rhinitis (Maskatia and Baker, 2010), leucopenia in a 51 year old woman who took 450 mg Echinacea capsules for 2 months (Kemp and Franco, 2002), thrombocytopenia with E. pallida in a 32 year old man (George et al., 2006) and hepatotoxicity in a 45-year old male who took 1,500 mg Echinacea root for the treatment of cold (Kocaman et al., 2008). However, limited information was available in these case reports about the doses taken, and it was uncertain whether the adverse effects described were related to Echinacea consumption or to other factors, such as the use of other herbal products such as St John's wort (Lee Soon and Crawford, 2001) or G