A Case of hepatotoxicity by Pelargonium sidoides

M.C. Lenti\textsuperscript{1,2}, A. Baldini\textsuperscript{3}, E. Cecchi\textsuperscript{2,3}, R. Bonaui\textsuperscript{1,2}, E. Gallo\textsuperscript{1,2}, A. Pugi\textsuperscript{1,2}, V. Maggini\textsuperscript{1,2}, F. Firenzuoli\textsuperscript{4}, N. Lombardi\textsuperscript{1,2}, E. Lucenteforte\textsuperscript{1,2}, M. Moschini\textsuperscript{1,2}, A. Mugelli\textsuperscript{1,2}, A. Vannacci\textsuperscript{1,2}

\textsuperscript{1}Department of Neurosciences, Psychology, Drug Research and Child Health (NEUROFARBA), University of Florence
\textsuperscript{2}Tuscan Regional Centre of Pharmacovigilance of Florence
\textsuperscript{3}Emergency Department, Prato's Hospital
\textsuperscript{4}Centre for Integrative Medicine, Careggi General Hospital, Florence, Italy.

Background
Pelargonium sidoides (PS) is an African herbaceous, perennial plant in the geranium family. The root is the medically part used for respiratory problems [1]. The reported pharmacological activities include moderate direct antibacterial and antiviral potencies and immunomodulatory properties. An alcohol extract of PS has become popular in Germany as a treatment for different respiratory problems, including acute bronchitis, the common cold, sinusitis, pharyngitis and tonsillitis. The chemical composition of the Pelargonium sidoides consists mainly of sesquiterpenes, the most abundant, coumarin and high quantity of tannins.

Case Presentation
In March 2011, a 46 year-old male patient was admitted to Emergency Department (ED) of Prato for severe asthenia associated to a wide complex tachycardia sensitive to intravenous amiodarone. The patient suffered from epilepsy, oligophrenia, hypothyroidism, hypertension and congenital heart disease. He had been on well tolerated therapy with furosemide, acetylsalicylic acid, phenobarbital sodium, carbamazepine, olanzapine, valproate sodium, lansoprazole, allopurinol, camrenone, for ten years. On admission, vital signs were normal except for heart rate (108 beats per minute) and pulse oximetry (oxygen saturation level of 91%). The blood tests, performed about 15 days before, showed normal values (especially ALT, AST and bilirubin were in normal range). Just before hospital admission, the patient was treated with a remedy for a common cold: PS 30 drops three times a day, stopped after six days. In ED the routine blood tests showed increased liver enzymes: ALT: 2385 IU I\textsuperscript{-1} (normal range: 1-45) and AST: 4072 IU I\textsuperscript{-1} (normal range: 1-36). After three days, blood tests showed a decrease of ALT: 1813 IU I\textsuperscript{-1} and AST: 1251 IU I\textsuperscript{-1} and INR (International Normalized Ratio): 1.89. The patient died the 4th day, probably due to acute liver failure and respiratory distress related to the above comorbidities. The PS causality assessment was defined as 'possible' according to Naranjo algorithm.

Discussion
Adverse drug reactions (ADRs) related to PS are quite rare in the published clinical trials and generally, they are of mild severity and comparable to placebo. The most frequent ADRs reported, due to PS, were gastrointestinal disorders, nervous system, ear and labyrinth disorders. It is known that high concentrations of coumarins and tannins can cause liver toxicity. Recently, 15 cases of suspected hepatotoxicity induced by PS has been published, but they were evaluated as 'doubtful' by the authors [2]. It is important to remember that concomitant diseases and drug interactions may have contributed to the above adverse event. Our case underlines the importance of further studies to establish the real association between PS and liver damage.