

# Abstract

**Background:** The use of herbal medicines in children and adolescents is continually on the rise. Contrary to popular belief, herbal products (HPs) are not always a safe alternative to conventional drugs and can cause a variety of adverse events such as severe and fatal allergic reactions. In regards to herbal medicine use in children, a recently published systematic review that searched PubMed, Embase, PsycINFO and AMED included 58 studies from 19 countries and found overall herbal lifetime use to be between 0.8–85.5 % and 2.2–8.9 % for current use. Unlike most synthetically produced drugs, the adverse event profile of such “natural” preparations in children has rarely been studied. To this date, effective systems that monitor adverse drug events (ADRs) and long term side effects associated with HPs are either non-existent or still developing in many countries. Due to insufficient and inconsistent ADR reporting, little is known about the ADR spectrum of herbals in pediatric patients. Awareness of the potential of HPs to cause ADRs, particularly in children and adolescents, needs to be increased and reporting to national pharmacovigilance centers (PVCs) reinforced.

**Objectives:** This project analyzed the worldwide adverse event data for herbal drugs related to hypersensitivity reactions as recorded in the WHO’s global individual case safety report (ICSR) database VigiBase® between 1968 and August 2014, focusing on pediatric patients under the age of 18 years.

**Methods:** From the original VigiBase® extract, only drugs with an herbal ATC code (HATC), classified as “suspect” with a *certain*, *possible* or *probable* causality assessment, a time of ADR onset of “0-1 day”, patient age less than 18 years and ADRs suggesting hypersensitivity, were included in this study. WHO-Art preferred terms indicating allergy were further divided into *allergic* and *asthma-like*.

**Results:** 26,909 ICSRs relating to herbal drugs worldwide, accounting for a total of 237,496 reported ADRs, comprised the original dataset. Of these 150 cases, representing 222 ADRs, met our study’s inclusion criteria. Out of 222 ADRs, 202 were classified as *allergic* and 20 as *asthma-like*. The most frequently reported WHO-ART terms in the allergic group were urticaria (22.1 %), rash (11.7 %) and anaphylactoid reaction (9.0 %). The most common reported terms of the *asthma-like* reactions were asthma (5.4 %) and

bronchospasms (2.7 %). Mixed herbals were the most frequently reported suspect herbal causing almost equally as many *allergic* (60.9 %) as *asthma-like* reactions (70.0%). Anaphylactic shock was reported in 12 cases (5.4 %) and no case was lethal. Most reports occurred in those 13-17 years of age. Males (54 %) were slightly more affected than females (46 %). The majority of cases were reported in Germany (28 %), Sweden (15.3 %) and Thailand (11.3 %).

**Conclusion:** Data analyzed as reported in VigiBase® showed that herbal medicines can cause severe hypersensitivity reactions and anaphylaxis in children and adolescents. To further optimize the usefulness of pharmacovigilance data and establish safer treatment regimens for pediatric patients, awareness of potential health threats through herbal medicines needs to be increased and the reporting of ADRs promoted.