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Ginkgo biloba extract safety: Insights from a real-world pharmacovigilance study of FDA adverse event reporting system (FAERS) events

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Highlights

- The real-world data shows that *Ginkgo biloba* extract is linked to 88 terms and 5,184 adverse reactions, raising global safety concerns.
- *Ginkgo biloba* extract caution is needed when prescribing it to patients with drug interactions.
- *Ginkgo biloba* extract is considered an early failure type due to its association with adverse drug events.

Abstract

Ethnopharmacological relevance

A traditional Chinese medicine extracted from the Ginkgophyta, *Ginkgo biloba* is commonly used to treat cardiac cerebral disease all over the world. Limited data exist regarding adverse drug reactions associated with *Ginkgo biloba* extract post-marketing.

Aim of the study

Currently, the drug safety profile of *Ginkgo biloba* extract is assessed using a substantial volume of case safety reports within the FDA Adverse Event Reporting System (FAERS) database.

Materials and methods

The study collected adverse events (AEs) data associated with *Ginkgo biloba* extract as the primary suspected drug from 2004 to 2023 from the FAERS database. A standardized mapping analysis of System Organ Class (SOC) and preferred term (PT) was conducted. Utilizing reporting odds ratio (ROR), proportional reporting ratio (PRR), information component (IC), and empirical Bayes geometric mean (EBGM), significant disproportionate measurement signals of adverse drug reactions (ADR) were identified and high-intensity signals were analyzed.

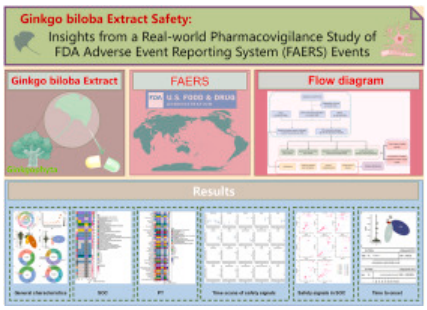
Results

700 reports of adverse events related to *Ginkgo biloba* extract were found in the FAERS database, affecting 23 organ systems. 88 significant mismatches were identified using four algorithms, leading to unexpected major adverse events like amaurosis fugax, fractional exhaled nitric oxide created, and obstructive sleep apnoea syndrome. The study observed a median onset time of AE associated with *Ginkgo biloba* extract at 7 days (interquartile interval [IQR] 0–109 days), with the majority of AE manifesting within the initial 7 days of drug treatment initiation. This investigation identified a noteworthy AE signal for *Ginkgo biloba* extract, underscoring the importance of clinical surveillance and risk assessment in its use.

Conclusions

In clinical practice, this study provides a deeper and broader understanding of suspected adverse reactions associated with *Ginkgo biloba* extract.

Graphical abstract



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Introduction

In recent years, influenced by the global trend of "healthy living",herbs (Poswal et al., 2019), fruits(Murali et al., 2021), vegetables(Ockermann et al., 2021), and other plant-derived substances(Stompor-Gorący et al., 2021) have been utilized for centuries due to their potential health benefits. Numerous studies support their use in supporting overall health and preventing diseases(Abdalla et al., 2021; Hikisz and Bernasinska-Slomczewska, 2021; Ramos-Romero et al., 2021). Thus, natural products can be considered as convincing candidates for daily diets and treatments as a result of their various health promoting properties.

Ginkgo biloba L. is one of the oldest extant tree species globally. It is a unique tree with no close relatives (Hohmann et al., 2018). *Ginkgo biloba* L. is widely planted for its ornamental value, and its leaves have significant medicinal benefits. Extracts from these leaves find applications in medicine, food, cosmetics, and more (Isah, 2015). *Ginkgo biloba* extract, a pale yellow powdery substance made from dried ginkgo leaves, contains phenolic acids, ginkgo terpene lactones, flavonoid glycosides among others, and has the ability to eliminate excessive free radicals in the body, adjust circulatory system function, improve hemodynamics, and protect tissues (Tian et al., 2017; Eisvand et al., 2020; Liu et al., 2022; Fan et al., 2024). The approved uses for *Ginkgo biloba* extract differ due to variations in local national policies. European herbal medicine guidelines outline the use of ginkgo-based products for improving the quality of life in patients with cognitive impairments and mild dementia (Tewari et al., 2018). According to the China Pharmacopoeia, the extract is indicated for cerebral and peripheral blood circulation disorders (Chan et al., 2007b; Shahrajabian et al., 2022). In recent years, due to its favourable effects and wide-scale use in treating cardiovascular and cerebrovascular diseases, *Ginkgo biloba* extract has gained popularity and is often the preferred choice of treatment (Nash and Shah, 2015; Yang et al., 2017). However, there is a common perception that traditional medicinal extracts are natural, safe, and without side-effects, especially as most traditional medicines are plant-based. Hence, while considering the therapeutic effects of drugs, the safety of *Ginkgo biloba* extract should not be neglected.

The FDA's Adverse Event Reporting System (FAERS) is a key tool for monitoring drug safety after it hits the market. It collects reports of adverse events from various sources globally, including ginkgo leaves and extracts (Raschi et al., 2018; Barvaliya et al., 2023), but there are limited and slow reports on their adverse reactions (Fransen et al., 2010a; Hoban et al., 2019). Therefore, this study leveraged the real-world AEs data in the FAERS database to compare safety aspects, analyze the signals of adverse drug reaction (ADR) disproportionality analysis for *Ginkgo biloba* extract, and explore unknown or potential signals. This study aims to provide a reference for rational clinical drug use.

Section snippets

Data source and research design

This study analyzed the risk of *Ginkgo biloba* extract using the FAERS database from 2004 to 2023, including data on adverse events for all indications. The search also included the active ingredient of the product to gather more comprehensive results from drug reports. The retrieved drug information is presented in Supplementary data Table S1. …

Data cleaning process

Following FDA guidelines in this study, we first purged duplicate records prior to statistical analysis. For records with identical CASEID, we selected …

General characteristics

The data screening and analysis process of this research is demonstrated in Fig. 1. From the FAERS, we extracted 19,877,614 AE reports from 2004 to 2023. Following the screening procedure, we identified 700 AEs reports related to *Ginkgo biloba* extract, involving 8585 PTs. Out of these, 5184 PTs are full of forward signals of ROR, PRR, IC and EBGM. As depicted in Fig. 2A, the global top five countries are Portugal (17.71%), Germany (15.00%), France (9.71%), the United States (7.00%) and China …

Discussion

Ethnography serves as a pivotal social science research method, focusing on the meticulous description and in-depth analysis of specific cultures or social groups. This approach relies heavily on immersive field observation, active participation, and comprehensive interviews to gather rich, firsthand data (Morse, 2016). The reporting of adverse reactions to *Ginkgo biloba* extracts provides insight into certain ethnographic factors. The data recorded in the FAERS reflects reactions reported not …

Conclusion

Our pharmacovigilance analysis of the FAERS database provides a comprehensive and systematic evaluation of the safety profile of *Ginkgo biloba* extract, highlighting the onset timing of AEs. We identified several common AEs, including cough, somnolence, increased blood pressure, hematuria, and degraded appendages, which are significant for clinical awareness. Furthermore, we observed the occurrence of AEs with high RORs and new AEs such as obstructive sleep apnea syndrome, elevated fractional …

CRediT authorship contribution statement

Yinhui Yao: Writing – original draft, Methodology. **Jingyi Zhao:** Methodology. **Chen Li:** Methodology. **Yan Chen:** Methodology. **Tianci Zhang:** Methodology. **Xianhui Dong:** Methodology. **Weijuan Gao:** Conceptualization. **Yazhen Shang:** Writing – review & editing, Conceptualization. …

Ethics statement

The study was exempt from ethics review. …

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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1 These authors have contributed equally to this work.

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