Haemorrhage due to Ginkgo biloba?

- About 20 detailed reports of haemorrhage (usually cerebral, ocular, or post-surgical) in patients using Ginkgo biloba extracts have been published. One-third of these patients were also taking drugs that increase the risk of bleeding (anticoagulants or antiplatelet drugs).

- Some substances contained in Ginkgo biloba have been shown to have an antiplatelet effect.

- In practice, patients with risk factors for bleeding (anticoagulant or antiplatelet treatment, surgery, etc.) should avoid using Ginkgo biloba extracts.

Extracts from the leaves of the Ginkgo biloba tree are marketed in a variety of formulations with differences in administrative status (a). In France, the best-known extract is Tanakan®, which corresponds to a standardised Ginkgo biloba leaf extract (24% of flavonoids and 6% of terpenoids, including ginkgolides) (1). Various "dietary supplements" are also marketed for different uses: as "vasodilators", to improve cognitive functions, reduce tinnitus, relieve lower limb arteri- al disease, etc. (2).

About twenty cases of haemorrhagic adverse effects linked to Ginkgo biloba extracts have been published in detail.

Potentially severe haemorrhage. These reports include eight cases of cerebral haemorrhage, four cases of ocular haemorrhage, and several cases of postoperative bleeding (2-11). Surgery was sometimes needed to remove a haematoma or stop bleeding (2). One case of cerebral haemorrhage was fatal (4).

Bleeding was reported in only three of these cases, and in all three cases bleeding time was reduced when Ginkgo biloba was withdrawn and increased again when Ginkgo biloba was reintroduced (2,7).

Uncertainties in the role of Ginkgo biloba. About one-third of these patients were also taking drugs that could poten- tially cause haemorrhage or interact with Ginkgo biloba: anticoagulants (warfarin), antiplatelet drugs (aspirin), and non-steroidal antiinflammatory drugs (ibuprofen) (b)(2-4,7,8,10).

Unfortunately, the reports are incom- plete: the composition of the extract used was not specified in more than half the cases; no information was provided in some cases on the duration of treatment or on Ginkgo biloba withdrawal after the patient began to haemorrhage. Coagu- lation status was not studied in most cases.

An antiplatelet effect (through inhibition of platelet activating factor, PAF) was observed with a mix of three ginkgolides given at doses of 80 mg and 120 mg to six healthy volunteers (12). This effect cannot be extrapolated to the Ginkgo biloba extracts used by patients, however, because the composition of the extracts was not specified in more than half the reported cases, and, when a standard- ised extract was specified, the ginkgolide content was only 3.1%, for a usual dose of 120 mg/day (i.e. a daily ginkgolide dose of less than 4 mg).

A small placebo-controlled study in 12 healthy volunteers, lasting 3 months, showed a slight inhibitory effect of 120 mg standardised extract on the synthesis of a platelet clotting factor (thromboxane B2) (13).

However, a double-blind placebo-con- trolling trial in 32 healthy volunteers showed no statistically significant differ- ence between 3 doses of standardised Ginkgo biloba extract (120 mg, 240 mg, and 480 mg/day) on coagulation status and platelet aggregation after 14 days of treatment (14). A double-blind placebo- controlled trial in 50 young healthy vol- unteers showed no statistically significant difference between 240 mg/day of standardised Ginkgo biloba extract (twice the usual daily dose) and placebo on coagulation status and platelet aggregation after 7 days of treatment (15).

In practice: caution. Cases of haem- orrhage in patients taking Ginkgo biloba, together with the known antiplatelet effect of some standardised Ginkgo biloba extracts, call for caution. The latest French summary of product characteristics for Tanakan® does not mention a risk of bleeding, but this risk is mentioned in Martindale The Complete Drug Reference (1,16).

Patients with risk factors for bleeding such as anticoagulant or antiplatelet ther- apy and surgery should avoid using Ginkgo biloba extracts. For an assessment of clinical efficacy, see Prescrire Int 91, p. 205 - Ginkgo and Alzheimer’s disease.