

Advisory Commission for Plant Preparations

Advice of 22 October 2020 emitted by the Advisory Commission for Plant Preparations concerning the use of the leaves of *Carica papaya* L. and its preparations as food supplements.

The Advisory Commission for Plant Preparations was asked by the Directorate-General Animals, Plants and Food of the Federal Public Service Health, Food Chain Safety and Environment to issue an advice about the safe use of food supplements containing the leaves of *Carica papaya* L. or its preparations.

Regarding the Royal Decree of 29 August 1997 concerning the manufacture of and trade in foodstuffs composed of or containing plants or plant preparations, and in particular Article 4, §4;

Considering that *Carica papaya* L. is mentioned on List 3 of the Royal Decree of 29 August 1997 (Plants to be notified if in a pre-dosed form) with the following restriction: Only the use of the following plant parts is permitted: "fruit";

Considering that *Carica papaya* L. is well known for its therapeutic and nutritional properties all over the world and that in literature, papaya leaf extract is confirmed to have strong medicinal properties¹;

Considering

- the study of Ekong M. B. et al, concluding "the aqueous leaf extract of *C. papaya* at the given dosage in this study is detrimental to developing fetuses, and these effects were dose dependent. Hence, the use of the extract especially during the period of gestation should be discouraged"²;
- the study of Nkeiruka U. E. et al, where the administration of methanol leaf extracts in male Wistar rats caused a significant reduction of spermatozoa count and increased the % of sperm cells that are defective when compared to the control³;
- the study of Akinloye O. O. and Morayo O. M., where a decoction of dried leaves was administered to male Wistar rats with the result that all of the andrological parameters investigated showed a significant reduction in mean values when compared with the control⁴;
- no data are available in literature to identify the process or substances responsible for the established reprotoxic effects;
- the presence of the alkaloid carpaine in the papaya leaves^{5, 6, 7, 8, 9};
- the possible presence of cyanogenic glucosides (a.o. prunasine) in the papaya leaves^{10, 11};

The Advisory Commission on Plant Preparations concludes that the leaf of *Carica papaya* L. and its preparations pose health risks and therefore should not be used in food supplements.

The Advisory Commission on Plant Preparations reserves the right to re-examine this advice in the light of new considerations.

Referenties

1. Singh, S.P., Kumar, S., Mathan, S.V. et al. Therapeutic application of *Carica papaya* leaf extract in the management of human diseases. DARU J Pharm Sci (2020).
2. Ekong, M.B. et al, "Morphometric Malformations In Fetal Rats Following Treatment With Aqueous Leaf Extract Of *Carica papaya*", Asian Journal of Medical Sciences 2 (2011) 18-22
3. Nkeiruka, U.E. et al, "Anti-fertility effects of *Carica papaya* Linn: Methanol Leaf Extracts in Male Wistar Rats", J. of Pharmacology and Toxicology 8 (1): 35-41, 2013
4. Akinloye O.O. et al, "Evaluation of andrological indices and testicular histology following chronic administration of aqueous extract of *Carica papaya* leaf in Wistar rat", African Journal of Pharmacy and Pharmacology. Vol. 4(5), pp. 252-255, May 2010
5. Haldar S., Mohapatra S., Singh R., Katiyar C.K. Isolation and quantification of bioactive Carpaïne from *Carica papaya* L. and its commercial formulation by HPTLC densitometry. Journal of Liquid Chromatography and Related Technologies 2020: p. 1-6.
6. Teng W.-C., Chan W., Suwanarusk R., Ong A., Ho H.-K., Russell B., Rénia L., Koh H.-L. In vitro antimalarial evaluations and cytotoxicity investigations of carica papaya leaves and carpaïne. Natural Product Communications 2019; 14 (1): 33-36.
7. Hornick C.A., Sanders L.I., Lin Y.C. Effect of carpaïne, a papaya alkaloid, on the circulatory function in the rat. Research Communications in Chemical Pathology and Pharmacology (1978) 22:2 (277-299).
8. Julianti T., Oufir M., Hamburger M. Quantification of the Antiplasmodial Alkaloid Carpaïne in Papaya (*Carica papaya*) Leaves. Planta Medica 2014; 80 (13): 1138-1142.
9. Zunjar V., Dash R.P., Jivrajani M., Trivedi B., Nivsarkar M. Antithrombocytopenic activity of carpaïne and alkaloidal extract of *Carica papaya* Linn. leaves in busulfan induced thrombocytopenic Wistar rats. Journal of Ethnopharmacology 2016; 181: 20-25.
10. Seigler D.S., Pauli G.F., Nahrstedt A., Leen R. Cyanogenic allosides and glucosides from *Passiflora edulis* and *Carica papaya*. Phytochemistry 2002; 60 (8): 873-882.
11. Olafsdottir E.S., Bolt Jorgensen L., Jaroszewski J.W. Cyanogenesis in glucosinolate-producing plants: *Carica papaya* and *Carica quercifolia*. Phytochemistry 2002; 60 (3): 269-273.