

## Opinion on elevated morphine levels in poppy seeds

February 8, 2006

### **Introduction**

Poppy seeds are the ripe seeds harvested from the capsules of *Papaver somniferum* L. (opium poppy, family: Papaveraceae). Owing to their content of fatty oil (40 – 60 %) and protein (15 – 24 %), the seeds have been a popular source of food (for example in poppy-seed cake, desserts etc.). In poppy seeds, in contrast to other parts of the plant, the alkaloid-rich latex (milky juice) is not found. Therefore, poppy seeds contain the alkaloids only in traces according to the scientific literature and have not been included in regulations under the Narcotics Act. Partially the same plants from which the seeds derive are used to obtain opium (dried latex from unripe capsules) or opium alkaloids. In addition to the primary alkaloid, morphine, there are secondary alkaloids such as codeine, thebaine, noscapine (formerly referred to as narcotine) and papaverine found in opium.

### **Case report (Germany, February 2005)**

To relieve high restlessness, a 6-week-old female infant was given an amount of about 75 mL of a mixture that had been prepared by boiling 500 mL milk with 200 g poppy seeds and adding some honey. The mother had followed a suggestion by an old home recipe published in a baking book in 2004. At about 23 h, the mother had given her baby the poppy seed infusion to have her sleep through the night. Three hours later, the infant's breath became very irregular with a rasping sound. She had to be brought to hospital by an emergency ambulance. On admission, the infant suffered from increasing respiratory insufficiency and had to be artificially respirated. Based on the manifestations observed, opiate poisoning was suspected at an early stage. The infant had to be administered six courses of an antidote until a stable spontaneous respiration could be restored. After 10 days, she could be discharged from hospital in a healthy condition.

The opiate poisoning was confirmed on the day of admission to hospital. Urine analysis revealed morphine and codeine levels of 18 000 and 317 µg/L, respectively. On the following day, the morphine level dropped to 627 µg/L and the codeine level, to below 5 µg/L. The morphine level in the blood serum was 4.3 µg/L on the following day. In the poppy seeds used, 0.1 % morphine and 0.003 % codeine were detected.

### **Analytical data on alkaloid levels in poppy seeds in Germany**

Already in 2002, the BgVV, the predecessor of the BfR, had pointed out that, from the viewpoint of food toxicology, need for action was seen insofar as data on the alkaloid levels in poppy seeds should be collected and appropriate examination performed. From September to November 2005, the BfR received analytical data obtained by food control authorities in analyses of poppy seeds commercially available in Germany. The evaluation of these data revealed a clear trend towards higher morphine (and codeine) levels when compared with the data published so far. Thus, in merely 13 out of 48 poppy seed samples tested, morphine levels detected were ≤ 10 µg/g, while in 9 samples, morphine levels detected were as high as > 100 µg/g up to a maximum of 330 µg/g. In contrast, the analytical data published before had revealed morphine levels of ≤ 4 µg/g in at least 50 % of samples and of more than 100 µg/g, namely 151.6 µg/g, in one case only. In addition to morphine and codeine, also noscapine, papaverine and thebaine were detected in poppy seeds in single examinations. Maximum limits for admissible levels of the above opium alkaloids in poppy

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seeds are only known to exist in Hungary. These are: 30 µg/g for morphine, 20 µg/g for noscapine, 40 µg/g for morphine + noscapine, 20 µg/g for thebaine, and 20 µg/g for codeine.

***Possible causes of high alkaloid levels in poppy seeds***

The possible causes of high opiate levels sometimes found in poppy seeds include the use of less appropriate botanical varieties and an unfavourable time of harvesting as well as certain geographical origins. For example, it is a striking fact that high morphine concentrations are frequently found in seeds originating from Australia. Another basic problem seems to consist in the contamination of poppy seeds with capsule fragments and latex both containing alkaloids. Thus, morphine levels could be drastically reduced by washing of the seeds. It has been assumed that the elevated morphine levels presently found in poppy seeds are to be attributed to newly introduced mechanical harvesting techniques.

***Risk potential***

The risk potential of the alkaloids with the main focus on morphine can be deduced from the data available because of pharmaceutical uses. Morphine has both central and peripheral effects. Central nervous effects include above all analgesia, euphoria, anxiolysis, sedation, clouding of consciousness, nausea, vomiting, respiratory depression and cardiovascular effects. Chronic use of morphine will result in tolerance and both mental and physical dependence. In animal studies, morphine has shown effects indicating developmental and reproductive toxicity, and in some studies, also genotoxic effects. The lowest therapeutic single oral dose of morphine sulfate pentahydrate is stated to be 2.5 mg (corresponding to 1.9 mg morphine). On principle, considerable variation in individual sensitivity has to be assumed with regard to the therapeutically desirable and undesired effects of morphine. It has become known both from findings of forensic examinations and from a consumer complaint that morphine uptake from poppy seeds through the consumption of common amounts may reach the order of magnitude of therapeutic doses and may cause adverse effects known from medical use. The German institutions responsible for official food control have raised corresponding objections (corresponding to Article 14 para 2a and para 4 of Regulation (EC) 178/2002, and reports to the EU Rapid Alert System for Food and Feed).

***Abuse of poppy seeds***

On the internet, instructions are available for illicit extraction of opium alkaloids from blue poppy seeds commercially available in Germany by means of citric acid. On such websites, there have also been reports stating that effects typical of morphine, such as euphoria, sedation and gastrointestinal complaints were observed after the consumption of such extracts.

***Exposure to poppy seeds***

The quantity of poppy seeds spread on bread rolls, bagels, muffins or similar bakery products will weigh normally 1 – 4 g/piece. Cakes are mostly prepared by boiling ground poppy seeds in milk and baking this mixture together with other ingredients. The share of poppy seeds as stated in common recipes is 10 – 30 %, where as a piece of cake from a bakery weighs about 150 – 200 g. In addition, poppy seeds are used in sweet dishes such as 'Mohnpielen', a traditional Silesian dessert, (up to 10 – 20 %) and sprinkled on pasta. In terms of amounts commonly consumed at once or distributed over the day, the intake of 50 g poppy seeds (ca. 1 piece of cake) is considered as a moderate intake, that of 100 g poppy seeds (ca. 2 pieces of cake), as a high intake, and that of 150 g poppy seeds (ca. 3 pieces of cake), as a worst-case intake.

***Assessment / recommendation by the BfR***

To provide the official food control authorities with qualified data to substantiate their decisions with regard to the limits of morphine concentrations in poppy seeds which can be accepted also from a precautionary angle, intake levels / guideline values for morphine concentrations in poppy seeds have been derived by the BfR.

Based on the lowest effective morphine dose stated for oral medication (i.e. 1.9 mg, corresponding to 31.7 µg/kg body weight for an individual of 60 kg body weight), and particularly with regard to

- the prevailing uncertainty concerning the threshold doses for health-relevant effects, above all for psychomotor effects,
- possible interactions e.g. with other opium alkaloids in poppy seeds, pharmaceuticals acting on the CNS and alcohol,
- the uncertainty concerning occupational safety and road-traffic safety resulting from the above-mentioned considerations,
- the interindividual variation in sensitivity to be expected, and
- a higher sensitivity associated with old age and numerous medical conditions,

the BfR has derived a 'provisional maximum daily intake'.

It is 6.3 µg morphine/kg body weight/day and determines the intake which an individual (as related to kg body weight) should not exceed per day when consuming foods containing poppy seeds, whether in a single meal or distributed over the entire day. Based on the provisional maximum daily intake and taking into account an estimate of the amounts consumed, a provisional guideline value of 4 µg morphine/g in poppy seeds was recommended. The manufacturers involved are requested to make every effort to reduce the concentrations of all pharmacologically active opium alkaloids in poppy seeds to the lowest level technologically achievable. The BfR recommends to have guideline values established also for codeine, noscapine, papaverine and thebaine on this basis.

Until a successful change in the manufacturing conditions of poppy seeds has been achieved, the BfR recommends to refrain from excessive consumption of foods containing high quantities of poppy seeds, particularly during pregnancy.

Annexes:

BfR Case report on Poppy Seeds

BfR Press release