

Report of the Scientific Committee of the Spanish Agency for Consumer Affairs, Food Safety and Nutrition (AECOSAN) in relation to the assessment of the exposure of the Spanish population to morphine resulting from the consumption of poppy seeds

Section of Food Safety and Nutrition

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Abstract

Poppy seeds (*Papaver somniferum*) are traditionally used in some countries in the manufacture of bread and cakes. In Spain, the dietary intake of these seeds is low and the variety of poppy mainly grown in the country is used to obtain morphine. Although poppy seeds do not contain opium alkaloids or these occur at very low levels, they may be contaminated with alkaloids, as a result of damage caused by certain insects or of the external contamination of the seeds during harvest if dust particles from the straw become attached to the seeds.

The Scientific Committee has conducted an assessment of the exposure of the Spanish population to morphine as a result of the intake of the varieties of poppy seeds grown in Spain and considers that, in accordance with currently available data, the intake of morphine as a result of the consumption of bread and cakes by the Spanish population is below the acute reference dose (ARfD) established by the European Food Safety Authority (EFSA).

The greatest uncertainty in this estimation comes from the lack of accurate information regarding the consumption of poppy seeds by the Spanish population. Both the morphine content in the poppy seeds, and the intake of these seeds could change in the future as a consequence of the improvement of good practices in the production and processing of the seeds or of an increased industrial or culinary use of the same in Spain.

Key words

Opium poppy, corn poppy, bread, morphine, pastries, *Papaver somniferum*.

1. Introduction

The opium poppy is the species *Papaver somniferum* L. (Papaveraceae), an annual herbaceous plant reaching 50-150 cm in height. The fruit is a spherical or ovoid capsule, on a stalk, which is swollen at the connection point. The ripened fruit opens by valves, located below the star-shaped stigma. The capsules contain numerous seeds, approximately 25 000 per capsule (Paris and Moyses, 1967) (Kuklinski, 2000). In addition to numerous hybrids grown in gardens, there are three crop varieties grown for medicinal or food purposes. *Papaver somniferum* var. *glabrum* Boiss., with purple or white flowers, white or dark purple seeds; *P. somniferum* var. *album* D.C., white flowers and yellow-white seeds; and *P. somniferum* var. *nigrum* D.C., purple flowers and slate-grey seeds. A fourth variety, *P. somniferum* var. *setigerum* D.C., with purple flowers and serrated leaves, is considered to be the wild form in the south of Europe and is not used for cultivation (Paris and Moyses, 1967) (Evans, 2009). The species *P. bracteatum* Lindl. is also used for pharmaceutical purposes, but its principal metabolite, thebaine, must be converted into morphine by semi-synthesis (Samuelsson, 1992), therefore the seeds of this species would not contain morphine but rather some other opium alkaloids. Opium poppy seeds are small (approximately 1 mm), kidney-shaped, covered by hexagonal indentations, and range in colour from dark grey to yellowish-white (Gill and Brandt, 1926). They are traditionally used in Central Europe and North America in the baking of bread and cakes, and although in their natural form they do not contain morphine or other opium alkaloids, these may appear attached as a result of the handling processes, and occasionally appear in significant quantities.

One of the problems observed at a commercial level is the confusion in the naming of the seeds from the common poppy (*Papaver rhoeas* L., *Papaveraceae*) and from the opium poppy, also known as papaver seeds. The first species does not contain opium alkaloids in its capsule or in the so-called straw. Therefore, the correct naming of the seeds used is necessary.

In 2011, the European Food Safety Authority (EFSA) assessed the risk for public health derived from the presence of opium alkaloids in opium poppy seeds. These are mainly used in the preparation of bakery products, on top of some dishes, in fillings in cakes and pastries and to produce edible oil. In the assessment carried out by the EFSA it was estimated that exposure to morphine derived from the intake of foods containing opium poppy seeds, could exceed the acute reference dose in some consumers, particularly children (EFSA, 2011). In order to avoid this risk and reduce the content of alkaloids in the seeds, the European Commission published in 2014 certain recommendations, which considered the application of good practices (EU, 2014).

In Spain, the main variety of opium poppy that is cultivated is for obtaining morphine, and therefore the presence of morphine in the seed may be far higher than that which appears in the seeds of varieties cultivated in other European regions where the seeds are used for culinary purposes. Therefore, the Management Board of the Spanish Agency for Consumer Affairs, Food Safety and Nutrition (AECOSAN) has asked the Section of Food Safety and Nutrition of the Scientific Committee to carry out an assessment of the exposure of the Spanish population to morphine as a result of the consumption of the varieties of opium poppy seed cultivated in Spain and to establish whether there may be a health risk.

2. Morphine in opium poppy seeds

Although opium poppy seeds do not contain opium alkaloids or these occur at very low levels, they may be contaminated with alkaloids, as a result of damage caused by certain insects or of the external contamination of the seeds during harvest if dust particles from the straw become attached to the seeds. Opium poppy seeds are traditionally used in Central Europe and North America in the manufacture of bread and cakes. On the plant, prior to harvest, the seeds do not contain morphine or other opium alkaloids, but contamination due to the handling of the capsules has resulted in the detection of variable quantities ranging from 4 mg/kg to 250 mg/kg (Bruneton, 2009).

The alkaloid content depends on various factors, observing a significant difference in those varieties intended for the pharmaceutical industry compared to those grown exclusively for the food sector. This may be one of the problems, as the morphine content of the variety cultivated in Spain is far higher than that of the varieties cultivated in other Member States. Moreover, certain Member States have national legislation establishing maximum limits for opium alkaloids. This situation generates notifications in the RASFF (Rapid Alert System for Food and Feed) and places the feasibility of the single market at risk, as the seeds produced in one Member State cannot be marketed in another.

In light of the above, a request has been made for the assessment of the exposure of the Spanish population to morphine as a result of the consumption of the varieties of opium poppy seed grown in Spain and to establish whether a health risk may exist.

The opiate content of opium poppy seeds is variable and depends on the origin of the seed and the processing method employed.

In Spain, the opium poppy is produced by one single business, mainly for use by the pharmaceutical industry. Since 2015, it has been applying Commission Recommendation (2014/662/EU) on good practices to prevent and reduce the presence of opium alkaloids in poppy seeds and poppy seed products (EU, 2014).

An overview of the analyses carried out in Spain of 200 different samples of seeds of *Papaver somniferum* produced in Spain between 2014 and 2016 reveals huge variability in the samples. The analyses carried out using HPLC-UV, reveal values ranging from 13.55 mg/kg (2015) to 596.00 mg/kg (2014 prior to the application of Commission Recommendation (2014/662/EU) on good practices to prevent and reduce the presence of opium alkaloids in poppy seeds and poppy seed products).

3. Consumption of opium poppy seeds in Spain

In Spain the consumption of opium poppy seeds is low and food intake surveys do not include the seed, making it far more difficult to determine the level of intake by the Spanish population and, therefore, to establish the potential risk posed by the consumption of morphine as a contaminant. However, in Central European countries extensive information is available regarding the consumption of seeds due to the influence of their contaminants on health. For example, two studies conducted in Hungary in 2003 and 2009 assessed the intake of morphine as a result of the consumption of contaminated seeds. Although the figures are estimated according to the

consumption of bread/cakes containing opium poppy seeds, the degree of contamination from previous analyses, and the reduction of the morphine content from the seed handling processes prior to its consumption, a possible daily intake of morphine through these foods has been estimated at between 18.3-25.4 and 25.6-47.4 µg/kg for adults and between 32.9 and 66.4 µg/kg for children, respectively (Zentai et al., 2012).

The import to Spain of opium poppy seed from different countries may provide data of reference. According to Eurostat, in 2015, 396.7 tonnes of seeds were imported to Spain from different countries. The 96 tonnes marketed in Spain in 2015 by the only Spanish company producing these seeds must be added to this quantity. In addition, 7 652.9 tonnes of seeds were exported from Spain to different countries in 2015 (Eurostat, 2016). However, these figures do not permit the quantity of opium poppy seeds consumed by the Spanish population to be estimated, as there is a commercial exchange that may include the reshipment of seeds imported to Spain to other countries.

The Spanish Federation of Food and Drink Industries (FIAB) has provided figures for the production of bread, cakes and pastries using opium poppy seeds by the association of Spanish businesses in this sector. In industrial pastries the seeds are mainly used as "topping" in percentages ranging from 0.87 to 2.5 % of the weight depending on the product, while in bread products the seeds may be used indistinctly as "topping" (0.1 to 5 %) or in the dough (0.09 to 0.97 %). In total, the six companies which provided data used almost 72 700 kg during 2015. Taking these figures, it is possible to establish a scenario for the consumption of opium poppy seeds in Spain.

Based on the percentages for the use of seeds in bread and cakes provided by the industry, it is possible to calculate the total quantity of product from each company that includes these seeds in its ingredients. For this, the lower of the percentages of use reported for bread (0.09 to 0.8 % according to the company) and for cakes (0.87 to 0.95 % according to the company) is taken, so that the production of product with seeds is overestimated and the worst-case scenario is obtained with regard to the possible intake of morphine. The quantity of product with seeds calculated amounts to 7 252.27 tonnes of bread and 370.75 tonnes of cakes.

Once the total quantity of bread and cakes/pastries with seeds produced by these companies has been estimated, this is compared with the total production of the companies declared by the Association of the Bread, Cakes and Pastry Industry in 2014 (718 000 tonnes of bread and 134 000 of cakes/pastries) (ASEMAC, 2015) in order to establish the percentage of the total production that contains seeds. Thus, it is estimated that the amount of bread containing opium poppy seeds is equivalent to 1.33 % of the total production of bread and that 0.28 % of the total production of cakes/pastries would also contain these seeds.

If these percentages for the production of bread/cakes containing opium poppy seeds are applied to the consumption of bread or cakes/pastries by the Spanish population according to different consumer surveys for different age groups (mean and P95 of ENALIA survey for 6-11 months, 12-35 months, 3-9 years and 10-17 years (AECOSAN, 2016) and adult surveys (AECOSAN, 2006)), the corresponding means and P95 are obtained for the consumption of bread and cakes/pastries containing poppy seeds (Tables 1 and 2).

The highest figure obtained for the consumption of bread containing poppy seeds of 3.99 g/day corresponds to the P95 of the 10-17 year-old age group in the ENALIA survey, whereas in the case of cakes/pastries the highest consumption is 0.83 g/day corresponding to the P95 (total of biscuits, cakes and pastries) in adults (Tables 1 and 2). By considering the intake of all types of bread and cakes/pastries, the consumption is overestimated in order to obtain the worst-case scenario.

Table 1. Estimation of the consumption of bread with seeds by age group

Age groups	Consumption of bread and similar products (only consumers) (g/day)		Consumption of bread with seeds (g/day)
Adults	Mean for white bread	92.3	1.23
	P95 for white bread	198.64	2.64
	Mean for wholemeal bread	39.92	0.53
	P95 for wholemeal bread	96.54	1.28
10-17 years	Mean	123.86	1.65
	P95	300	3.99
3-9 years	Mean	79.7	1.06
	P95	200	2.66
12-35 months	Mean	34.7	0.46
	P95	100	1.33
6-11 months	Mean	12.42	0.17
	P95	42.72	0.57

Table 2. Estimation of the consumption of cakes/pastries with seeds by age group

Age groups	Consumption of cakes/pastries (only consumers) (g/day)		Consumption of cakes/pastries with seeds (g/day)
Adults	Mean for biscuits	31.04	0.09
	P95 for biscuits	72.82	0.20
	Mean for cakes	51.18	0.14
	P95 for cakes	123.06	0.34
	Mean for pastries	47.23	0.13
	P95 for pastries	104.78	0.29
10-17 years	Mean	78.30	0.22
	P95	194.53	0.54
3-9 years	Mean	64.79	0.18
	P95	165.39	0.46
12-35 months	Mean	33.46	0.09
	P95	95.18	0.27
6-11 months	Mean	12.84	0.04
	P95	30	0.08

Applying the highest seed content percentage (%) reported by the companies (5 % in bread and 2.5 % in cakes) to the consumption of bread and cakes/pastries containing seeds, a maximum consumption of opium poppy seeds is obtained per person of 0.2 g/day from bread (children aged 10-17 years old and adults) and 0.02 g/day from cakes/pastries (for adults). Again, by applying the highest seed percentage the consumption is overestimated in order to obtain the worst-case scenario. In spite of this, the estimated intakes are far lower than those given by the EFSA for Central European countries in their opinion on the presence of opium alkaloids in opium poppy seeds (EFSA, 2011).

4. Exposure to morphine as a result of consumption of opium poppy seeds in Spain

Nevertheless, as indicated above, it is currently very difficult to determine the exact intake of opium poppy seeds in Spain. It is possible to calculate the exposure to morphine of the Spanish population from the figures for morphine content and for the estimated seed intake.

For this exposure calculation, in the worst-case scenario, the maximum content of morphine in seeds produced in Spain may be considered (a figure from 2014, 596 mg/kg) and the estimation of the consumption of seeds calculated by applying the highest seed content percentage reported by the companies (5 % in bread and 2.5 % in cakes) to the consumption of bread and cakes/pastries. By using the highest morphine content observed, the morphine content is also overestimated in order to give the worst-case scenario.

With these figures, for the highest group of consumers of bread and cakes/pastries, the intake of morphine from bread and similar products would be 0.12 mg morphine/day (children aged 10-17 years and adults) and from cakes/pastries would be 0.01 mg morphine/day (for adults).

Considering the body weight reported in the food intake surveys used, the highest intake of morphine would be in the 12-35 month age group with an intake of 3.58 µg/kg b.w./day resulting from the sum of the bread and cake/pastries (Tables 3 and 4).

Table 3. Estimation of morphine intakes through the consumption of bread by population of different age groups

Age groups	Consumption of bread with seeds (g/day)	Consumption of seeds (g/day)	Morphine intake (mg/day)	Body weight (kg)	µg morphine/kg b.w./day
Adults	3.93	0.2	0.12	68.5	1.75
10-17 years	3.99	0.2	0.12	50.5	2.38
3-9 years	2.66	0.13	0.08	26.0	3.08
12-35 months	1.33	0.07	0.04	12.3	3.25
6-11 months	0.57	0.03	0.02	9.0	2.22

Table 4. Estimation of morphine intakes through the consumption of cakes/pastries by population of different age groups

Age groups	Consumption of cakes/pastries with seeds (g/day)	Consumption of seeds (g/day)	Morphine intake (mg/day)	Body weight (kg)	µg morphine/kg b.w./day
Adults	0.83	0.021	0.013	68.5	0.19
10-17 years	0.54	0.014	0.008	50.5	0.16
3-9 years	0.46	0.010	0.007	26.0	0.27
12-35 months	0.27	0.007	0.004	12.3	0.33
6-11 months	0.08	0.002	0.001	9.0	0.11

In the assessment carried out by EFSA in 2011, an acute reference dose (ARfD) of 10 µg morphine/kg b.w. was established as a guidance value for morphine considering the nature of the short-term effects and because there is unlikely to be a carcinogenic or genotoxic potential derived from dietary exposure to opium poppy seeds (EFSA, 2011).

As indicated above, in the case of the Spanish population, the highest morphine intake would be in the 12-35 month age group with an intake of 3.58 µg/kg b.w./day resulting from the sum of bread and cakes/pastries. This estimated morphine intake would be far below the acute reference dose (10 µg morphine/kg b.w.) established by the EFSA.

Conclusions of the Scientific Committee

In accordance with the currently available data and the estimation made, the intake of morphine through the consumption of bread and cakes/pastries by the Spanish population is below the acute reference dose (ARfD) established by the EFSA.

The Scientific Committee recommends that the Commission Regulation on good practices to prevent and reduce the presence of opium alkaloids in poppy seeds and poppy seed products continues to be applied, in order to potentially obtain a minimum 10 % reduction in the morphine content.

In addition, the correct definition of the product is essential, avoiding the use of the word “poppy” instead of opium poppy when the species used is *Papaver somniferum*. The use of the term papaver is also inappropriate. It is recommended that the labelling of the product clearly indicates the origin of the seeds: Poppy for the species *Papaver rhoeas*, Opium poppy for *Papaver somniferum*) or a combination of both should indicate Poppy (*Papaver rhoeas*) and Opium Poppy (*Papaver somniferum*).

Uncertainties

The greatest uncertainty in this estimation comes from the lack of accurate information regarding the consumption of opium poppy seeds by the Spanish population. The consumption has been estimated based on production data provided by the bread and cake/pastries industry. There are other recent industrial uses of these seeds such as their addition to yoghurts, but given that the

estimations made have always tried to represent the worst-case scenarios, it is considered that, at present, the intake from these products is low and is covered by the estimation made.

Consumption is also possible as a result of a culinary use by consumers who purchase the seeds or by local bakeries and cake shops. This consumption does not appear to be highly relevant when considering the Spanish population as a whole given there is no tradition of a wide gastronomic use of these seeds in Spain. In addition, the reduction in the morphine content that may take place during the processing of foods containing the seeds has not been considered.

Both the morphine content in the opium poppy seeds, and the intake of these seeds could change in the future as a consequence of the improvement of good practices in the production and processing of the seeds or of an increased industrial or culinary use of the same in Spain.

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