

RESEARCH ARTICLE

The Risk of Using Poppy Seed Tea Made from Several Varieties Available on the Romanian Market

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Objective: the number of alkaloids like morphine and codeine found in poppy seeds used in food industry are monitored by a directive given by European Food Safety Authority. Based on this regulation the aim of the study was to determine the quantity of morphine and codeine from several brands of poppy seeds. **Methods:** an HPLC-UV method (205 nm) was developed to measure the quantity of morphine and codeine. Sample preparation was made using recipes posted on Drugs Forum by some users. Limits of detection were not determined because the lowest concentration from the reference (0.1 µg/ml) detected morphine concentrations that are far lower than a limit of toxicological concern. **Results:** The concentrations, which were found, ranged between Below the Level of Toxicological Concern (BLTC) - 243.26 mg/kg for morphine and BLTC - 88.58 mg/kg for codeine using several methods of preparation. **Conclusions:** one can observe that there are some brands of poppy seeds which do not respect the regulation about the amount of morphine and codeine. The high amount of morphine in some samples suggests that there are different varieties of poppy seeds, which can be used for an illicit purpose and can lead to addiction or even overdose in some cases.

Keywords: HPLC, morphine, codeine, regulations, poppy seeds

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Introduction

Morphine is one of the principal ingredients of opium, a drug that has been, by far, one of the most popular and commonly used and abused drug in human history [1]. Nowadays, it is an opiate narcotic painkiller with a high potential for abuse. It belongs to narcotic medication as can cause addiction, overdose and even death [2]. The drug can be used in clinical pain relief but it can be also used illicitly for recreational purpose among drug users. Once administered, the substance enters the blood stream which carries it to different parts of the body and in brain where it activates opioid receptors. While some effects are beneficial like pain relief due to the activation of μ_1 receptors subtype, others are unwanted such as respiratory depression and addiction due to activation of μ_2 receptors subtype. Because of its severe effects the substance is regulated worldwide in different classes of risks and it is not available without a medical prescription [3].

Even if the abuse of morphine is no longer as common as in the 19th century [4], drug users search for different methods to obtain morphine without a medical prescription. One of the most popular methods is obtaining morphine from poppy seeds [5]. Drug addicts sustain that making a poppy seed tea is the best solution to obtain doses of morphine large enough for the euphoric effect [6]. However, the concentration of morphine in poppy seed tea can vary enormously so the risk of an overdose is high especially when it is taken with other drugs like benzodiazepines, a combination very popular among the drug con-

sumers [7]. Unfortunately, there are death cases reported worldwide because of the overdoses found in poppy seed tea. One of the cases found on the internet showed that the overdose appeared when using 1.5 kg of poppy seeds for obtaining the tea. Furthermore, it was an unexpected and undesired effect because the consumer had taken poppy seed tea several times, always using the exact amount of seeds and the same preparation method [8].

Based on The European Food Safety Authority's document about the alkaloids present in the poppy seeds used in food industry, we analysed the amount of morphine from several poppy seeds types available in our country.

The European Food Safety Authority (EFSA) Panel on Contaminants in the Food Chain (CONTAM Panel) established a safety factor of 3 to obtain from the lowest known single oral therapeutic dose of 30 µg morphine/kg body weight (b.w.) an acute reference dose (ARfD) of 10 µg morphine/kg b.w. The safety factor of 3, applied by the EFSA in the case of morphine takes into consideration the acute toxic effect, the lowest active pharmacological dose ever published and the size and type of the population exposed to the substance [9].

The aim of this study was to determine the amount of morphine and codeine in poppy seed tea, made from different types of poppy seeds, by four different infusion methods, in order to evaluate if there is a possibility that these poppy seeds can be used for a recreational purpose. We also intended to verify if the regulations regarding the procedures of decreasing the number of alkaloids are taken into consideration. Literature data shows that using the poppy seeds tea for recreational purpose is an easily available and high risk method for opioid users [10].

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Materials and methods

1.1. Equipment and reagents

Merck HPLS system consisting of: quaternary pump Merck Hitachi L-7100, auto sampler Merck Hitachi L-7200, column thermostat Merck Hitachi L-7360, detector de DAD Merck Hitachi L-7455, interface Merck Hitachi D-7000 I/F, solvent degasser Merck Hitachi L-7612, D-7000 HSM- Manager software, LichroCART 250-4, Rp- Select B (5 µm) column Merck KgA, Germany.

The following reagents were used: purified water (Millipore, USA), H₃PO₄ and K₂HPO₄ (Merck KgA, Germany), morphine hydrochloride (analytical purity), codeine phosphate (analytical purity); commercially available poppy seeds (countries of origin: Romania, Czech Republic, Spain and Turkey).

1.2. HPLC method

The mobile phase composition, gradient and flow rate are shown in Table I.

The injection volume was 100 µl and the full "loop" method was used.

DAD domain: 190-400 nm, best chromatogram extracted at 205 nm, because this wavelength gives the best signal-to-noise ratio. Peak purity limit: 95%. Analyse time: 15 minutes.

Retention time:

- morphine 6.70 minutes;
- codeine 10.03 minutes.

1.3. Preparation of the samples

Analyzed poppy seeds recipes are shown in Table II. Four types of sample preparation were used to reproduce recipes taken from Drugs Forum which are provided by some consumers [10].

For a better extraction of alkaloids, an acidic medium (pH = 3) was used for sample preparation. Until analysis, the samples were frozen at -20°C. There were used four methods of preparation: in the first one the seeds were sim-

ply washed, in the second one they were left in contact with the extraction solvent and washed, for the third method the seeds were grinded before the washing procedure and for the fourth method the poppy seeds were grinded and left 24 hours in contact with the extraction solvent. After defrosting at room temperature, samples were centrifuged 5 minutes at 5000 rpm, filtered through a 0.5 µm nylon filter and injected into the HPLC system.

1.4. Method performance testing

1.4.1. Specificity

To assess the specificity of the method we used a sample of poppy seeds without detectable concentrations of codeine and morphine. All methods of sample preparations showed no peaks with the retention times of morphine and codeine. A typical chromatogram of a sample is shown in Figure 1.

1.4.2. Linearity

To assess the linearity of the method, the following concentration ranges were chosen (N = 3):

- morphine 0.1-15 µg/ml
- codeine 0.1-15 µg/ml

The coefficient of correlation (R) was 0.998 for morphine and 0.998 for codeine (Figure 2). All the residuals (difference between the calculated-from the calibration curve – and theoretic concentration, expressed as a percent of the theoretic concentration) were under 10%. Representing the residuals as a function of the theoretic concentration, no correlating tendency was found.

1.4.3. Accuracy and precision

Spiked sample technique, of a poppy seed type that was found to have undetectable concentrations of morphine and codeine, was used for assessing the accuracy and precision of the method. Three values of concentrations were used (5 mg/kg, 20 mg/kg, 60 mg/kg of poppy seeds, N = 5). Recovery ranged between 81.13-95.30% and the coefficient of variation ranged between 0.28-0.45%. Similar results were obtained in the case of codeine, too.

1.4.4. Limit of detection and quantification

The limit of detection and quantification were not determined. In the case of morphine any peak lower than the lowest point of the calibration curve (0.1 µg/ml corresponding to 1 mg/kg poppy seed) was considered far below of the range of toxicological concern (EFSA RfD would

Table I. HPLC pump setup

Time (min)	Methanol (%)	20 mM phosphate buffer, pH = 3 (%)	Flow rate (ml/min)
0	5	95	1.000
8.0	30	70	1.000
15.0	30	70	1.000
15.1	5	95	1.000
17.0	5	95	1.000

Table II. The methods of preparation

Series 1	Series 2	Series 3	Series 4
-0.3 g poppy seeds homogenized with 3 ml phosphate buffer pH = 3 -vortex for 1 minute -the solution was centrifuged at 5000 rpm for 5 minutes -the samples were frozen	-0.3 poppy seeds homogenized with 3 ml phosphate buffer pH = 3 and left to rest for 24 hours -vortex for 1 minute - the solution was centrifuged at 5000 rpm for 5 minutes -the samples were frozen	-0.3 g grinded poppy seeds homogenized with 3 ml phosphate buffer pH = 3 -vortex for 1 minute -the solution was centrifuged at 5000 rpm for 5 minutes -the samples were frozen	-0.3 g grinded poppy seeds homogenized with 3 ml phosphate buffer pH = 3 and left to rest for 24 hours -vortex for 1 minute - the solution was centrifuged at 5000 rpm for 5 minutes -the samples were frozen

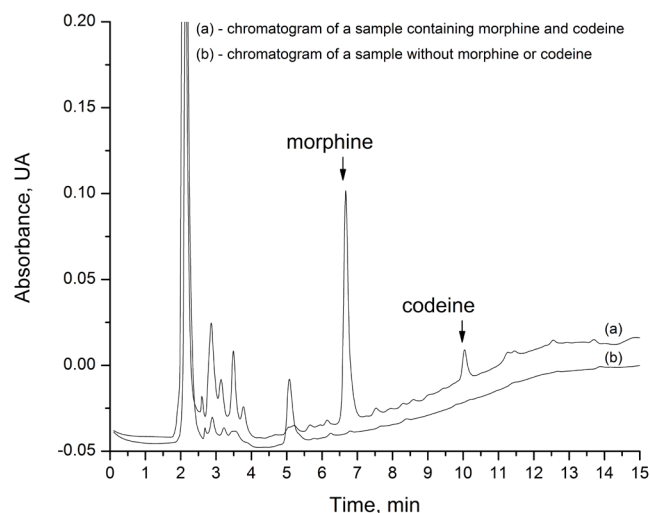


Fig. 1. Comparative chromatogram of a poppy seed tea sample without morphine and codeine, and another one containing both analytes

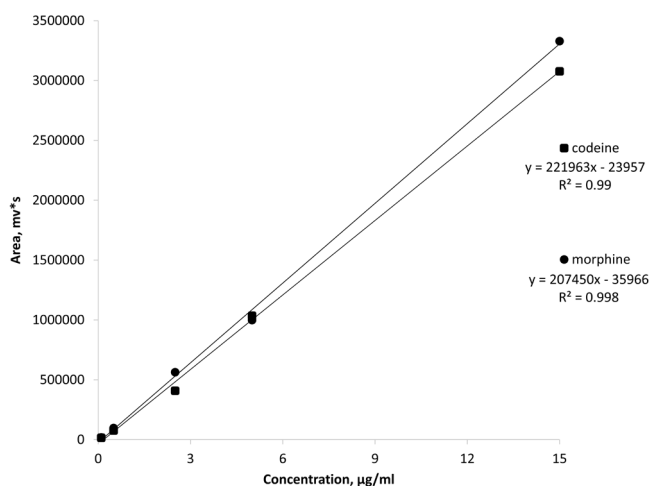


Fig. 2. The linearity curves of morphine and codeine

Table III. The concentration of morphine and codeine from the different types of poppy seeds (mg/kg morphine / mg/kg codeine)

Sample number	Series 1	Series 2	Series 3	Series 4
1	0.10/BLTC	2.04/3.83	1.30/BLTC	22.47/88.58
2	13.75/0.22	3.39/BLTC	0.91/BLTC	8.08/BLTC
3	37.03/0.77	44.16/BLTC	13.86/BLTC	29.06/BLTC
4	0.44/BLTC	2.73/BLTC	BLTC/BLTC	13.30/BLTC
5	0.81/0.26	3.06/BLTC	BLTC/BLTC	28.85/BLTC
6	112.41/16.50	243.26/28.80	117.77/10.51	119.16/9.00
7	7.00/BLTC	8.94/BLTC	8.03/BLTC	42.26/BLTC
8	30.70/3.76	124.84/12.18	98.26/6.59	59.52/BLTC
9	3.82/BLTC	29.90/BLTC	12.00/BLTC	49.43/BLTC
10	8.80/BLTC	15.25/BLTC	4.52/BLTC	29.22/BLTC
11	6.95/0.30	9.61/BLTC	6.81/2.03	11.88/BLTC

Abbreviation: BLTC - Below of Toxicological Concern

be found in 3 kg poppy seeds) and its concentration was noted with BLTC (Below the Level of Toxicological Concern) The codeine is 10 times less potent than morphine, therefore this concentration is even less importation.

Results

Concentrations of morphine and codeine measured in the samples are shown in Table III.

Concentrations for morphine ranged between 0.1 - 112.41 mg/kg for series 1, 2.04 - 243.26 mg/kg for series 2, BLTC - 117.77 mg/kg for series 3 and 8.08 - 119.16 mg/kg for series 4. In the case of codeine the concentrations ranged between BLTC - 16.50 mg/kg, BLTC - 28.80 mg/kg, BLTC - 10.51 mg/kg and BLTC - 88.58 mg/kg, for the series 1, 2, 3 and 4, respectively. For the preparation of the poppy seeds tea, quantities of 200-2000 g seeds are most often used.

Discussions

From the results presented above it is obvious that some of the poppy seed cultivars, easily available on the supermarkets, can be dangerous for human health if they are used in the production of poppy seed tea. Some of the studied samples can produce an overdose and can be possibly deadly (series 1, 2, 4). Even if none of the brands analysed does not contain a quantity of morphine which can have a recreational effect if used as food, there is a high possibility of recreationally use the tea produced from certain seeds. Even overdose and death can result if certain seeds are used in the highest amount recommended by some users for poppy seed tea preparation. Moreover, the methods of preparation are simple and the seeds can be bought freely, therefore, it is obvious that a drug with high addictive and toxic potential can be obtained with very little effort in the lack of a restrictive legislation.

Codeine concentrations in all samples are very low, even undetectable in many cases, and could not be considered to contribute to a recreational or toxic effect of the samples we analysed.

Conclusions

The HPLC method we propose is suitable to detect and measure the quantity of morphine and codeine from the poppy seeds. The method can be used even in emergency situations to confirm the presence of morphine and codeine in liquids suspected to be poppy seed teas. Even if presence of codeine observed in all of our measurements is not of any toxicological concern, its presence can be used to differentiate solutions obtained from analytical purity morphine from those obtained by washing poppy seeds.

Large variation of the morphine content observed in our samples is a high risk of overdose and death especially for young people trying to prepare a poppy seed tea in the lack of a certain degree of tolerance. The presence of samples with such high amounts of morphine suggests that some

poppy seed producers might not wash their products as requested by European authorities.

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Conflict of interest

None declared.

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