

A Review: production of Poppy Seed in Afghanistan and its Composition Effects

ABSTRACT

The main aim of this study is poppy plant with two important compounds of that poppy seed and opium which those are produced and used by people of world especially in a poor country like Afghanistan, the poppy seed used in bakery products, in pastry filling in deserts and the production of edible oil, also opium used as a drug. These contain morphine, thebaine, papaverine, codeine and narcotic which 20%, 1%, 1%, (5-8)% respectively. According to, Bozan, B., & Temelli, F. the proximate analysis of poppy seed shown the low content of moisture that is 5.3%, high content of crude fat 49.9% also it has ash, carbohydrate, and crude protein by percentage of 5.1%, 18.3%, and 21.6% respectively. As well as they include practically all essential amino acids, except for tryptophan, and are high in oil, carbs, calcium, and proteins. Poppyseed and opium as used for increasing the economic situation of the government of Afghanistan while surveys by (UNODC) from 2000 to 2020 in metric tons per year, the production of poppy seed increase from 3200 to 8200. The risk of addiction to opium smoking appears to be slightly lower than that of parenteral heroin use, but significantly higher than that of alcohol. Even in countries where its use is common, opium smoking poses significant health and social risks.

Keywords: poppy plant, poppy seed, opium, drug, alkaloids compound

1. INTRODUCTION

Poppy seeds are derived from opium poppy seeds (*Papaver somniferum* L.). They are used in bakery products, pastry fillings, desserts, and the production of edible oil. Narcotic alkaloids such as morphine

and codeine are part of the opium poppy plant (López et al., 2018). Poppy was used as a substitute for bread. In this category, two groups were known: plants with elongated capsules and seeds; and plants forming involute and elongated capsules with black seeds. *Papaver somniferum* is the seed's botanical name. *Papaver hybridum* is the next group's botanical name (Simmonds.,1976). There are many varieties of this poppy species, the opium poppy, *Papaver somniferum*, is the type of poppy from which opium and all refined opiates such as morphine (up to 20%), thebaine (5%), papaverine (1%), codeine (1%), and narcotine (5-8%) are naturally present and extracted from the poppy (Nargiz et al., 1994). In addition to minerals and water-soluble vitamin content, the proximate chemical composition of poppy seeds has been investigated. The following composition (440 g kg⁻¹), protein (211 g kg⁻¹), moisture (50 g kg⁻¹), ash (63 g kg⁻¹), crude fiber (62 g kg⁻¹), and total carbohydrates were shown in the proximate study of poppy seeds (236 g kg⁻¹). The predominant elements in the poppy seeds were potassium and calcium. The largest unsaturated fatty acid (750 g kg⁻¹ total fatty acids) was linoleic acid, while the main saturated one was palmitic acid (86.4 g kg⁻¹). The quantities of α -, fl- and tocopherols contained in poppy seed oil were respectively 220 μ g g⁻¹, 40 μ g g⁻¹ and 20 μ g g⁻¹. Pantothenic acid was found at the highest level among the water-soluble vitamins listed, followed by niacin and thiamine (Schwartz et al., 1985). Opium was essentially an undisputed commodity at the beginning of the nineteenth century. Such was its value as a drug that people must have interpreted "opium of the people" in the first years of the nineteenth century as something we might translate as "penicillin of the people" into a twentieth-century idiom. By the end of the century, however, other drugs had largely supplanted its medicinal uses, and opium was practically demonized by medical and moral puritans. Marx penned opium as his symbol for religion in these two ages. It is an ambiguous, multidimensional, and contradictory metaphor in 1843 that reflects both the earlier and later understandings of the poppy seed (McKinnon et al.,2005). (poppy) is an annual crop grown in countries such as China, India, Czechoslovakia, and Turkey. Poppy is cultivated primarily because of its opium and oil content. The seeds are primarily used to produce edible oil. The Oil content of poppy was reported to range from 45 to 50%. Poppy oil has approximately 10% palmitic, 73% linoleic, and 13% oleic acid as the major fatty acids. In Europe and Turkey, poppy seeds are mainly used for the health benefits of oils rich in linoleic acids, such as maize or safflower oils, in reducing serum cholesterol concentrations. Sweets, such as sesame seeds, are commonly used for baking and sprinkling on rolls and bread, and edible oil is often extracted from poppy seeds. Poppy seeds are also used in pastry making locally (Gök et al.,2011). About 90 % of morphine is excreted in the urine within 24 hours mainly as M3G (up to 60 %), M6G, and only 2-12 % is excreted as morphine unchanged. since 80 % is present in the ionized form. Small amounts of morphine glucuronides are excreted in the bile, recirculated enterohepatically, resulting in another 7-10 % of the dose of morphine being excreted in faeces. The elimination half-life of morphine is approximately 120 minutes in humans. Morphine is distributed

throughout the body, mostly (65 %) found in the kidneys, liver, GI tract, lungs, and spleen, while lower levels (20 %) are present in the brain and muscles. Though the brain is its primary site of action, morphine does not cross the blood-brain barrier easily. Following intravenous administration, morphine has an apparent volume of distribution ranging from 1 to 4.7 L/kg. Protein binding is reported to be 36 % and muscle tissue binding is reported to be 54 %. Morphine diffuses across the placenta, and traces also appear in milk and sweat. Morphine glucuronides are subject to active transport out of as is morphine via the P-glycoprotein in the human GI tract, but apparently not the brain (Alexander et al., 2011).

2.REVIEW OF LITERATURE

Poppy appears to be one of the few plants that were used and even cultivated in ancient times. The origin, however, is not yet conclusively established and there are numerous claims in the literature about its first appearance. Before *Papaver Setigerum*, D.C., 1930. (Bernath et al., 1999). The alkaloids produced by the opium poppy latex (milky sap) include the narcotic agent's morphine and codeine, which have been used by humans to ease extreme pain for centuries. (EFSA., 2011). The spread of poppy was aided by the expansion of the Roman empire. Following the Roman era, the plant was cultivated in both European and Asian countries. India, Iran, and Afghanistan, in particular, are Asian countries. (Simmonds,1976).

Papaver somniferum (poppy) is grown as an annual crop in China, India, the Czech Republic, and Turkey. The poppy is grown primarily for its opium and oilseeds. The poppy seed (*Papaver somniferum* l.) is a vital oilseed that has a long history of cultivation in the Czech Republic. Because the poppy seed grown in the Czech Republic is of high quality, it is preferred above poppy seeds grown in other parts of the world. The purpose of this study is to describe the current state of Czech poppy seed production and international trade. Poppy yields can range from 1.8 to 2.9 tons per acre in theory. (Prochazka et al., 2012).

3.ALKALOIDS COMPOUND OF POPPY SEED

CODEINE

Codeine is an old pain reliever that is still routinely prescribed for mild to moderate pain. It is primarily metabolized via glucuronidation, but N-demethylation to norcodeine and O-demethylation to morphine are minor routes(Sindrup *et al.*,1995). Codeine is commonly prescribed in clinical treatment, with over the counter (OTC) versions readily available for use in cold/cough medications. We provide the first case of severe confessionals condition in a previously healthy 14-year-old girl, which was eventually linked to improper codeine usage. The use of codeine in the paediatric environment has come under scrutiny in recent years as a result of numerous reported deaths, most of which were caused by respiratory depression

(Reilly et al 2015). Increased sucrose association with our study improves codeine's ability to elicit analgesia. Both a decrease and an increase in analgesia might be observed. When compared to saline solution, experiences boost the anti-inflammatory pain generated by carrageenan. Control represents an increase in CNS delivery that may be possible. When Peripheral Inflammatory Pain is Exacerbated - Minduced Inflammatory Pain Codeine analgesia results in greater dosages of codeine being delivered to the CNS (Hau et al.,2004).

THEBAINE

Gum opium contains morphine, codeine, and thebaine. (Wu, C. Y., and J. J. Wittick,1977).

Thebaine is a naturally occurring opiate that enters the body with morphine and codeine. Because of the utilization of poppy seeds, there was a high possibility of being morphine and/or codeine positive, according to research. 3,4 To distinguish between an opiate positive due to morphine or codeine and a possible legal outcome of an opiate positive, laboratories in the drug testing and forensic sectors must discern between an opiate positive due to morphine or codeine (**Fathabadi, Motahare Vakili, et al.,2020**).

PAPAVERINE

The risk-benefit ratio of papaverine therapy has been difficult to determine; both the reliability and durability of papaverine-induced artery dilatation appear to be less definite than that accomplished by angioplasty. Clinical response to papaverine has been reported to be as low as 25%. A better understanding of the elements that influence a vessel's reaction to papaverine infusion would allow for better stratification of the treatment's expected utility, and hence a better description of the drug's risk: benefit ratio. The responsiveness of a spastic artery to the vasodilatory effects of papaverine appears to be dependent on the length of the spasm (8–10), according to studies in different animal models. A rabbit model of cerebral vasospasm was used to test the hypothesis. demonstrated that the response to papaverine was excellent for the first three days following induction of vasospasm, but that from day three today nine after induction of spasm, there was a steady deterioration in responsiveness to papaverine. The response to papaverine was reduced 10 to 14 days after induction of vasospasm in a canine model, compared to 4 to 7 days after induction of vasospasm. These findings show that early in vasospasm, smooth muscle contraction is the etiology of arterial constriction; subsequently, arterial wall fibrosis, edema, inflammation, or intimal proliferation are more likely causes of artery narrowing. (Mary E. Jensen, and Jacques E. Dion.,1997). Another opium poppy alkaloid, papaverine, is a smooth muscle relaxant used to treat cerebral and peripheral ischaemia, as well as cardiac ischaemia worsened by arrhythmias, according to Kallmes, David F(Peter, Kuruppacharil V., et al., 2012).

MORPHINE

Morphine levels in commercially available poppy seed and seed cake, as well as urine from healthy normal human adults 3 and 15 hours after ingestion of poppy seed cake, were detected. The concentrations of morphine found were as follows: between 374 51 and 9.4 1.0 mol kg⁻¹ poppy seed of different brands, 290 11 mol kg⁻¹ poppy seed paste, 1.43 0.07 and 0.53 0.15 mol litre⁻¹ urine sampled 3 and 15 h after ingestion of two cakes, respectively, and 0.67 0.17 and 0.30 0.06 mol litre⁻¹ urine sampled 3 and 15 h after ingestion of one cake. It is concluded that a positive finding of morphine in the urine from a person suspected of heroin abuse calls on some attention due to possible accidental morphine intake from poppy seed food. The opioids codeine, morphine, and heroin are all made from opium poppy resin. Morphine and codeine are medications that are used to treat severe pain, drowsiness, acute pulmonary edema, cough, and diarrhea. Heroin (diacetylmorphine) is a more potent version that is used to get a "high" illegally. (Kaye, A. D., & Urman, R. D. (Eds.).2011). All three opiates are converted to morphine glucuronide in the liver and eliminated in the urine. Except for codeine, relatively little medication is excreted in its whole. The opiates examined for are predominantly codeine and morphine in a drug-screening program to eradicate opiate misuse within a restricted group, which uses frequent, random, unannounced urine collection. The morphine concentration of poppy seed, which is extensively utilized in Central European foods and pastries, has recently aroused serious concerns. The morphine concentration of poppy seed, which is extensively utilized in Central European cuisine and pastries, has recently sparked widespread concern. Intoxication cases resulting from the intake of highly contaminated poppy seed prompted a discussion concerning maximum limitsPoppy seed with a morphine level of greater than 10

mg/kg was deemed unfit for human consumption in toxicological research conducted by the Bavarian State Office for Health and Food Safety (Sproll et al.,2007).

Table (1): Major Composition Found in poppy seed and their usage

No	Poppy Composition	Density (avg%)	Molecular formula	Molecular weight (g/mol)	Usage in Pharmacy	Comment	References
1	Morphine	11.4	$C_{17}H_{19}NO_3$	285.34	Narcotic analgesic	Major alkaloid of opium which is also a controlled substance.	Wang, J. K. (1977).
2	Codeine	3.5	$C_{18}H_{21}NO_3$	299.4	Analgesic and antitussive	Liver enzymes, most notably CYP2D6, convert codeine into morphine following oral ingestion. Codeine is thus a morphine prodrug. Codeine is a prohibited substance as well.	Vora, A., & Nadkar, M. Y. (2015), Demirkapu, M. J., & Yananli, H. R. (2020).
3	Thebaine	3.2	$C_{19}H_{21}NO_3$	311.4	Precursor of opioids	Thebaine is a morphine biosynthetic intermediate utilized in the production of oxycodone, oxymorphone, buprenorphine, and naloxone in the pharmaceutical industry. Thebaine is a prohibited substance as well.	Dasgupta, A. (2019).
4	Noscapine (narcotine)	8.1	$C_{22}H_{23}NO_7$	413.4	Antitussive	This substance could have anti-cancer capabilities. Noscapine is an unrestricted substance.	SEGAL, M. S,et al. (1957)

5	Papaverine	3.1	$C_{20}H_{21}NO_4$	339.4	Antispasmodic	Papaverine is not a controlled substance.	Ko, W. C. (1980).
---	------------	-----	--------------------	-------	---------------	---	-------------------

UNDER PEER REVIEW

Proximate analysis of poppy seed

Figure (1) has shown the proximate composition of a poppy seed that highest compound has to belong to crude fat which content 49.9, and the lowest belong to a moisture content that is (5.3) estimated. Ash, carbohydrate, and crude protein content are (5.9), (18.3), and (21.6) respectively.

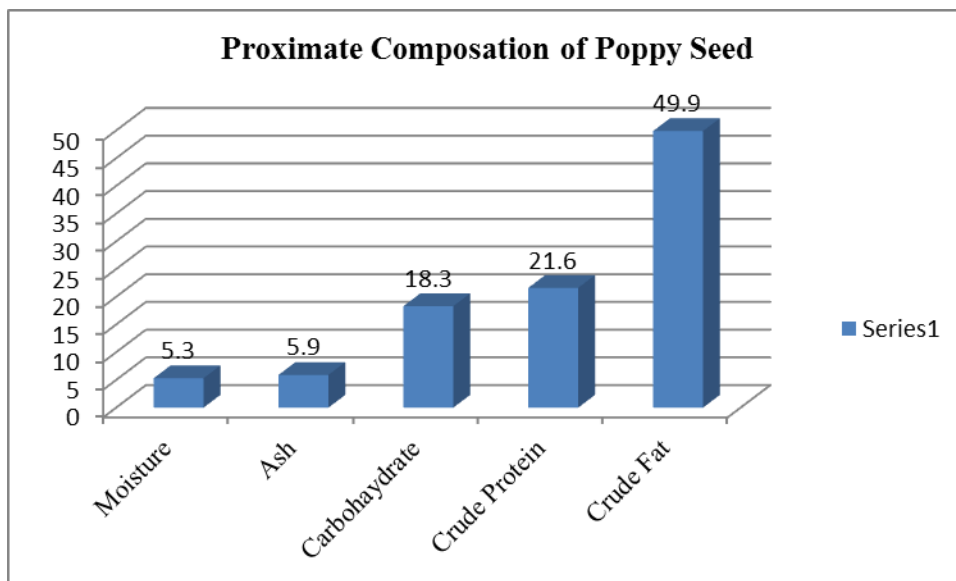


Fig (1): Proximate and analysis of poppy seed (Bozan, B., & Temelli, F.2008).

4. UTILIZATION OF POPPY SEED AS DRUG

The opium plant should be the center of any ethnobotanic or economic research of Papaver. Popov (1970) points out that, while all members of the Papaveraceae are poisonous in some way, *Papaver somniferum* L. is the most useful. The opium poppy plant, which was well-known in ancient Greece for its hypnotic properties, was first thought to be a magical or dangerous plant utilized in religious rites, only to later be used in healing. The nourishing seed was used as a hypnotic in milk; opium mixed with rose oil was used for headaches and eyedrops; it was used to arthritics (as were the leaves), and it was used to cure wounds and erysipelas when mixed with vinegar. Poppy could yield a range of useful meals due to its narcotic effects. Poppy seeds are pulverized for porridge and used in cakes and pastries as a filling or glaze. They include practically all essential amino acids, except tryptophan, and are high in oil, carbs, calcium, and proteins (Bhown, Shah and Nath, 1965) (Duke, James A, 1973).

The use of opium poppy as a medicinal plant has been described in Ayurveda since Bhavaprakasha (the ancient text/literature of 1600AD). In Ayurveda, opium, which is dried latex obtained from plant capsule,

is used after processing, as purified opium for pain management, treating dysentery, diarrhea, etc.(Mani, D., & Dhawan, S. S. 2011, February) as The use of honey is highly beneficial for the treatment of irritating cough, it most valuable to maintain healthy teeth and gums(Hasam, S *et al.* 2020).

Table (2): Usage of poppy seed in some industries

Sr. No.	Kind of industries	Poppy seed In (%)	References
1	Food	30	Blahovec ., (2002)
2	Oil	45	zan, B., & Temelli, F. (2008).
3	Bakery	40	Blahovec ., (2002)

5.USAGE OF DRUGS IN AFGHANISTAN

Drug addiction, as well as accompanying health difficulties (e.g., hepatitis C and overdose), and also some social and economic implications, are major concerns in Georgia today. Drug usage has risen dramatically since the early 1990s for a variety of reasons. On the one hand, the fall of the Soviet Union was followed by the collapse of a particular anti-drug system for the totalitarian state based on prohibitive measures. Handmade opium and the dried poppy solution were misused before 1998–99. Heroin has remained at the top of the list of injectable drugs since 1999–2000. Poppy seed misuse was rampant in 2003, but it was curtailed once preventative measures were implemented. In recent years, the misuse of buprenorphin (Subutex) has taken on new dimensions. Although Subutex is meant to treat opiate addiction, the way it is being utilized in Georgia is highly dangerous. Subutex is administered by the intravenous injection of non-sterile tablets that have been dissolved in boiling water. Subutex is usually used in groups in Georgia. Typically, the solution is prepared in a single vessel and shared by several individuals (Todadze., et al 2008). Nearly three decades of continuous violence have tarnished Afghanistan's recent history, culminating in the Taliban's ouster and the ongoing presence of international soldiers. Afghanistan's transition as the world's leading producer of illegal opium occurred during this period. When opium was first brought to Afghanistan, no one knows for sure. Someplace the introduction of opium poppies to the time of Alexander the Great, when his armies passed through Afghanistan on their way to India around 300 BC, while others date it to the time of the Muslim advance eastward through Afghanistan around the 7th or 8th century AD. After the Soviet troops left in 1989 and the communist government fell apart in 1992, Afghan fighters continued to use opium as a source of funding. Throughout the 1990s, the various warlords and factions fighting in Afghanistan wreaked even more havoc on Afghan infrastructure and traditional sources of livelihood, increasing Afghanistan's economic

reliance on opium. Any attempt to do so would risk open conflict in much of rural Afghanistan, which the Kabul government simply cannot risk. The effects of opium on Afghanistan's economy are unclear, and the country's economy is further complicated by the country's ongoing conflict. The fact that opium and its derivatives account for 40-60% of Afghan GDP, according to the Committee on International Relations, demonstrates the extent of Afghanistan's reliance on the illicit drug trade (Crumm, Jared., 2003). Opium's effects are essentially the same as morphine's, but unexpected side effects, such as oesophageal cancer associated with "dross opium" and polyneuropathy caused by deliberate arsenic addition, is a problem in some areas. The same factors that govern the use of alcohol and other drugs in western countries, such as ease of availability, price, and social acceptance, govern the prevalence of use in different areas and countries. The risk of addiction to opium smoking appears to be slightly lower than that of parenteral heroin use, but significantly higher than that of alcohol. Even in countries where its use is common, opium smoking poses significant health and social risks (Kalant, Harold., 1997).

6.OPIUM PRODUCTION IN AFGHANISTAN

According to the executive summary of the Afghanistan Opium Survey 2020, the total area under opium poppy cultivation in Afghanistan in 2020 was roughly 224,000 hectares, a 37 percent increase (or 61,000 hectares) over 2019. The area under cultivation, at 224,000 hectares, was among the largest ever observed.

Afghanistan's National Statistics and Information Authority (NSIA) and the United Nations Office on Drugs and Crime (UNODC) jointly issued the survey.

While the area under cultivation expanded in all of the country's major opium poppy-growing provinces, the South-Western region remained the country's leading opium producer, accounting for 71% of total opium production. In 2020, the country's total number of poppy-free provinces fell from 13 to 12, with Kapisa Province in the northeast losing its classification. The total amount of opium that might be produced was estimated to be 6,300 tons based on the information gathered. Researchers faced unprecedented challenges collecting data during COVID-19. Because in-person field work was not possible during the current epidemic, NSIA and UNODC developed and implemented a new approach based on satellite data to estimate yields. In 2020, the farm-gate value of opium harvest was predicted to be US\$ 350 million, which is a key indicator for farmers' overall revenue from opium growing. Farm-gate prices were at their lowest level since the commencement of the monitoring, at US\$ 55 per kilogram, indicating that the economic situation for impoverished opium producers may soon worsen.

Political instability, a scarcity of economic possibilities, a lack of quality education, and limited access to markets are all factors that contribute to opium poppy production in Afghanistan. Information cited from:

https://www.unodc.org/unodc/frontpage/2021/May/afghanistan_-37-per-cent-increase-in-opium-poppy-cultivation-in-2020--while-researchers-explore-novel-ways-to-collect-data-due-to-covid-19.html

The global poppy seed market was worth USD 183.9 million in 2020 and will be worth USD 214.5 million by the end of 2027, with a CAGR of 2.6 percent between 2022 and 2027. Information cited from: <https://www.360researchreports.com/enquiry/request-sample/17659686>

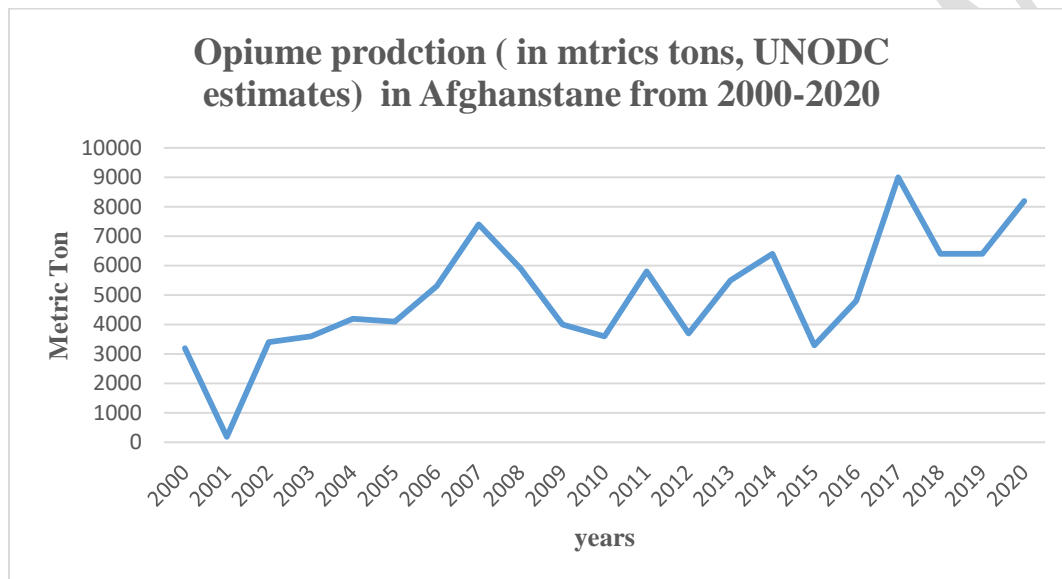


Fig (2): Opium production in Afghanistan

CONCLUSION

The poppy plant is used in the manufacturing of oil, as well as in pharmacies, bakeries, and as a medicine. Alkaloids that are most important Codeine, morphine, papaverine, Thebaine, and Noscapine (narcotine, which affects the mesocorticolimbic dopaminergic system) are some of the compounds found in poppy seeds. Dopamine is crucial in opioid consumption and maintenance, as it moves from the ventral tegmental region to the nucleus accumbens and medial prefrontal cortex. The proximate analysis of poppy seed shown a low content of moisture that is 5.3%, high content of crude fat 49.9% also it has ash, carbohydrate, and crude protein by percentage of 5.1%, 18.3%, and 21.6% respectively. Also, it has a good health effect for treatment of, treating dysentery, diarrhea, etc.

REFERENCES:

1. The global poppy seed market was worth USD 183.9 million in 2020 and will be worth USD 214.5 million by the end of 2027, with a CAGR of 2.6 percent between 2022 and 2027.
2. Nergiz, Cevdet, and Semih Ötles. "The proximate composition and some minor constituents of poppy seeds." *Journal of the Science of Food and Agriculture* 66.2 (1994): 117-120.
3. Schwartz, Robert S., and Katherine O. David. "Liquid chromatography of opium alkaloids, heroin, cocaine, and related compounds using electrochemical detection." *Analytical Chemistry* 57.7 (1985): 1362-1366.
4. McKinnon, Andrew M. "Reading Opium of the People': Expression, Protest and the Dialectics of Religion." *Critical Sociology* 31.1-2 (2005): 15-38.

5. Gök, Veli, et al. "Effect of ground poppy seed as a fat replacer on meat burgers." *Meat science* 89.4 (2011): 400-404.
6. Alexander, Jan, et al. "Scientific Opinion on the risks for public health related to the presence of opium alkaloids in poppy seeds." *EFSA JOURNAL* 9.11 (2011).
7. Bernath, Jenő, ed. *Poppy: the genus Papaver*. CRC Press, 1999.
8. EFSA Panel on Contaminants in the Food Chain. "Scientific Opinion on the risks for public health related to the presence of zearalenone in food." *EFSA Journal* 9.6 (2011): 2197.
9. Prochazka, Petr, and Lubos Smutka. "Czech Republic as an important producer of poppy seed." *Agris on-line Papers in Economics and Informatics* 4.665-2016-44881 (2012): 35-47.
10. Sindrup, Søren H., and Kim Brøsen. "The pharmacogenetics of codeine hypoalgesia." *Pharmacogenetics* 5.6 (1995): 335-346.
11. Reilly, David O., Mathew Thomas, and Edina Moylett. "Cough, codeine and confusion." *Case Reports* 2015 (2015): bcr2015212727.
12. Hau, Vincent S., et al. "Effect of λ -carrageenan-induced inflammatory pain on brain uptake of codeine and antinociception." *Brain research* 1018.2 (2004): 257-264.
13. Wu, C. Y., and J. J. Wittick. "Separation of five major alkaloids in gum opium and quantitation of morphine, codeine, and thebaine by isocratic reverse phase high performance liquid chromatography." *Analytical chemistry* 49.3 (1977): 359-363.
14. Fathabadi, Motahare Vakili, et al. "Synthesis of Magnetic Ordered Mesoporous Carbons (OMC) as an Electrochemical Platform for Ultrasensitive and Simultaneous Detection of Thebaine and Papaverine." *Journal of The Electrochemical Society* 167.2 (2020): 027509
15. Bernath, J. (Ed.). (1999). *Poppy: the genus Papaver*. CRC Press.
16. Mary E. Jensen, and Jacques E. Dion. "Infusing doubt into the efficacy of papaverine." *American Journal of Neuroradiology* 18.2 (1997): 263-264.
17. Peter, Kuruppacharil V., ed. *Handbook of herbs and spices*. Elsevier, 2012.
18. Sproll, Constanze, et al. "Guidelines for reduction of morphine in poppy seed intended for food purposes." *European Food Research and Technology* 226.1-2 (2007): 307-310.
19. Duke, James A. "Utilization of papaver." *Economic Botany* 27.4 (1973): 390-400.
20. Blahovec, J. "Mechanics of poppy seeds." *International Journal of Food Properties* 5.2 (2002): 277-287.
21. Todadze, Khatuna, and Gela Lezhava. "Implementation of drug substitution therapy in Georgia." *Central European journal of public health* 16.3 (2008).
22. Crumm, Jared. "Coca, Poppies, Kalashnikovs, and Cash: Illicit Drug Cultivation and Impacts of Anti-Drug Policy." (2003).

23. Dasgupta, A. (2019). Analytical True Positive: Poppy Seed Products and Opiate Analysis. In *Critical Issues in Alcohol and Drugs of Abuse Testing* (pp. 449-462). Academic Press.
24. Kalant, Harold. "Opium revisited: a brief review of its nature, composition, non-medical use and relative risks 1." *Addiction* 92.3 (1997): 267-277.
25. Wang, J. K. (1977). Analgesic effect of intrathecally administered morphine. *Regional Anesthesia: The Journal of Neural Blockade in Obstetrics, Surgery, & Pain Control*, 2(3), 3-8.
26. Vora, A., & Nadkar, M. Y. (2015). Codeine: a relook at the old antitussive. *Journal of The Association of Physicians of India*, 63(4), 80-82.
27. SEGAL, M. S., GOLDSTEIN, M. M., & ATTINGER, E. O. (1957). The use of noscapine (narcotine) as an antitussive agent. *Diseases of the Chest*, 32(3), 305-309.
28. Ko, W. C. (1980). A NEWLY ISOLATED ANTISPASMODIC-BUTYLIDENEPHTHAHDE. *The Japanese Journal of Pharmacology*, 30(1), 85-91.
29. Kaye, A. D., & Urman, R. D. (Eds.). (2011). *Understanding pain: What you need to know to take control*. ABC-CLIO.
30. Bozan, B., & Temelli, F. (2008). Chemical composition and oxidative stability of flax, safflower and poppy seed and seed oils. *Bioresource Technology*, 99(14), 6354-6359.
31. Demirkapu, M. J., & Yananli, H. R. (2020). Opium Alkaloids. *Bioactive Compounds in Nutraceutical and Functional Food for Good Human Health*.
32. Bozan, B., & Temelli, F. (2008). Chemical composition and oxidative stability of flax, safflower and poppy seed and seed oils. *Bioresource Technology*, 99(14), 6354-6359.
33. Mani, D., & Dhawan, S. S. (2011, February). Scientific basis of therapeutic uses of opium poppy (*Papaver somniferum*) in Ayurveda. In *International Symposium on Papaver 1036* (pp. 175-180).
34. Hasam, S., Qarizada, D., & Azizi, M. (2020). A Review: Honey and Its Nutritional Composition. *Asian Journal of Research in Biochemistry*, 34-43.
35. <https://www.360researchreports.com/enquiry/request-sample/17659686>
36. https://www.unodc.org/unodc/frontpage/2021/May/afghanistan_-37-per-cent-increase-in-opium-poppy-cultivation-in-2020--while-researchers-explore-novel-ways-to-collect-data-due-to-covid-19.html