



# *Opium for the Masses*

## **An Experimental Archaeological Approach in Determining the Antiquity of the Opium Poppy**

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*Abstract* The opium poppy, *Papaver somniferum* L., constitutes one of the most widely exploited psychoactive substances in human history. Hitherto, the investigation of the antiquity of the opium poppy's use by humans for narcotic purposes has predominantly relied on implicit archaeological data that suggests, but does not demonstrate such a use. In acknowledgment of the various geochemical processes involved in the creation, preservation, and decomposition of residues in archaeological contexts, an experimental archaeological approach was utilized to model the degradation of opium alkaloids. Procedures of the controlled creation, artificial aging, and the molecular characterization by gas chromatography/mass spectrometry of opium residues are presented. Experimental results and implications are also discussed.

*The opium poppy*, *Papaver somniferum* L., constitutes one of the most widely exploited psychoactive substances in human history. The diversity within the modern species, the fact that no truly wild variety exists, and the fact that several narcotic opiate compounds are commercially produced and distributed globally highlight the extent of the relationship which humans have maintained with this plant (Booth 1996:1–2; Flückiger and Hanbury 1879:45–50; Hammer and Fritsch 1977:120–124; Kapoor 1995:xi; La Valva et al. 1985:191, 195; Merlin 1984:18; Veselovskaya in Merlin 1984:35, 54, 73). Moreover, the isolation of morphine and the subsequent synthetic derivation of heroin have resulted in addiction in unprecedented numbers and corresponding efforts for regulation (Dupsák 1998:vii; Kalant 1997:267–268). The evaluation of the early use of this plant for narcotic purposes has been further complicated by its many non-narcotic uses, the interpretation of archaeological evidence, and limited understanding of the long-term preservation of the plant's compounds (Merlin 1984:20–6). For these reasons, traditional palaeobotanical methods have proven insufficient in approaching the antiquity of the narcotic use of opium.

The potential of applying chemical analytical techniques to such archaeological problems has long been acknowledged. In recent years, the chemical analysis of ancient residues has assumed a complementary role in traditional archaeological research programs with experimental work in the artificial creation of residues constituting a fundamental component (Eerkens 2005:98–99; Heron and Pollard 2008:9–11; Malainey 2007:88). The experimental aspect of this kind of research has proved successful in elucidating the various processes involved in the creation, preservation, and degradation of residues in archaeological contexts. The benefit of this approach is that it creates a baseline for the identification of organic products in archaeological contexts. However, the range of biochemicals to which these methods have been applied has remained limited. Emphasis has been placed on the analysis of plant and animal lipid compounds (primarily fatty acids) (Barnard et al. 2007:41; Eerkens 2005:89; Lambert 1997:164–166). This focus is understandable in that lipids are hydrophobic and therefore experience relatively little breakdown in archaeological contexts in comparison to other biological compounds. The primary disadvantage of lipid analysis is that it is non-specific, providing limited information about specific plant or animal species or genera and relegating research to subsistence products (Barnard et al. 2007:41–42; Derham 2004:187–90; Evershed 2000:204–207; Malainey 2007:77; Rafferty 2007:179).

For these reasons, an increasing number of residue analysts have started tar-

getting another class of compounds: alkaloids. Alkaloids are small, nitrogen-based organic molecules that frequently occur in plants and are “distinguished by their remarkable physiological activity” (Hesse 1981:2; Kapoor 1995:241–2; Roberts and Wink 1998:2–3). Unlike lipids, individual alkaloid compounds are limited in their distribution, making the identification of a particular species possible. Moreover, the fact that we can chemically identify alkaloids means that we have the potential to recover the more intangible aspects of human behavior through scientific methods (Hesse 1981; Rafferty 2007:179; Waterman 1998:87–88).

This paper presents the results of experimental research on opiate alkaloids. In order to gain a greater understanding of the prehistoric use of opium, the degradation of its chemical compounds, and its identification in archaeological contexts, a series of opium mixtures were artificially created and degraded. The procedures, results, and implications are described below.

### *The Opium Poppy: Botany, Pharmacology, and Uses*

*Papaver somniferum* L. is characterized by the production of a milky juice or latex, four-petaled flowers, and a capsule-like fruit that produces numerous seeds (Flückiger and Hanbury 1879:45–50; Hammer and Fritsch 1977:120–124; Kapoor 1995, 19, 20–24, 116–118; Merlin 1984, 29; Veselovskaya in Merlin 1984:35, 54, 73. See Figure 1). *Papaver somniferum* is one of two species that produce morphine (Kapoor 1995: 20; Levy and Milo 1998:93). The second species, *Papaver setigerum*, is a semi-wild variety. The great antiquity of the human exploitation of the opium poppy is demonstrated by the fact that a truly wild variety no longer exists, as well as by the unresolved evolutionary relationships between the two aforementioned species (Husain and Sharma 1983:3, 20; Levy and Milo 1998:93–94; Petri and Mihalik 1998:40–42).

As shown in Figure 2, it is unclear whether there was a linear development from the wild form to *Papaver setigerum* culminating in *Papaver somniferum*, whether they developed bilaterally via natural and artificial selection, respectively, or whether *Papaver setigerum* resulted from the abandonment of the cultivated form (Booth 1996:3; Hammer and Fritsch 1977:120–124; Kapoor 1995:9–10, 20; Merlin 1984:47–52; Veselovskaya in Merlin 1984:35, 54, 73). This produces a broad range of forms within and between varieties. The morphological features that most readily demonstrate the effects of human manipulation relate to the anatomy of the capsules, which tend to be larger with accelerated maturation

**Figure 1.** *Papaver somniferum* (Köhler, Franz Eugen, Hermann Köhler, Wilhelm Brandt, Marx Gürke, G. Pabst, Gustav, Schellenberg, and Max Vogtherr. 1897. *Köhler's Medizinal-Pflanzen in naturgetreuen Abbildungen mit kurz erläuterndem Texte: Atlas zur Pharmacopoea germanica*. <http://books.google.com/books?id=jecnAAAAAYAAJ&ots=bJargGx8xR&dq=K%C3%B6hler%E2%80%99s%20MedizinalPflanzen%20in%20naturgetreuen%20Abbildungen%20mit%20kurz%20erl%C3%A4uterndem%20Texte%3A%20Atlas%20zur%20Pharmacopoea%20germanica.&lr=&pg=PA9#v=onepage&q&f=false> (accessed October 20, 2011).



and lack holes that permit the dispersal of the seeds (Kapoor 1995:45–51; Wulff in Merlin 1984:47; Veselovskaya in Merlin 1984:40, 46–49). Such features would maximize the yield of narcotic or subsistence products.

Pharmacologically, the exceptional characteristic of *P. somniferum* is that the latex-producing capsule yields over forty alkaloids. This abundance of constituents translates to a broad range of pharmacological actions and therefore a broad range of medicinal uses (Hesse 1981:3–4; Kapoor 1995:162; Merlin 1984:92; Meyers 1896 in Hesse 1981:2–3; Siegel 1989). Of particular significance is the most active and abundant alkaloid, morphine, which dissipates “the anxiety associated with pain,” promotes therapeutic sleep, reduces hunger and fever, treats diarrhea and heart failure, and produces “mild euphoria and pleasant hallucinations” (Merlin 1984:91). Excessive doses may result in nausea, convulsions, or death. Additional effects may manifest from interactions between alkaloids (Husain and Sharma 1983:131–133; Merlin 1984:92).

Besides morphine, the alkaloids that occur in the largest quantity and highest concentration and that produce the greatest physiological effects (and thus

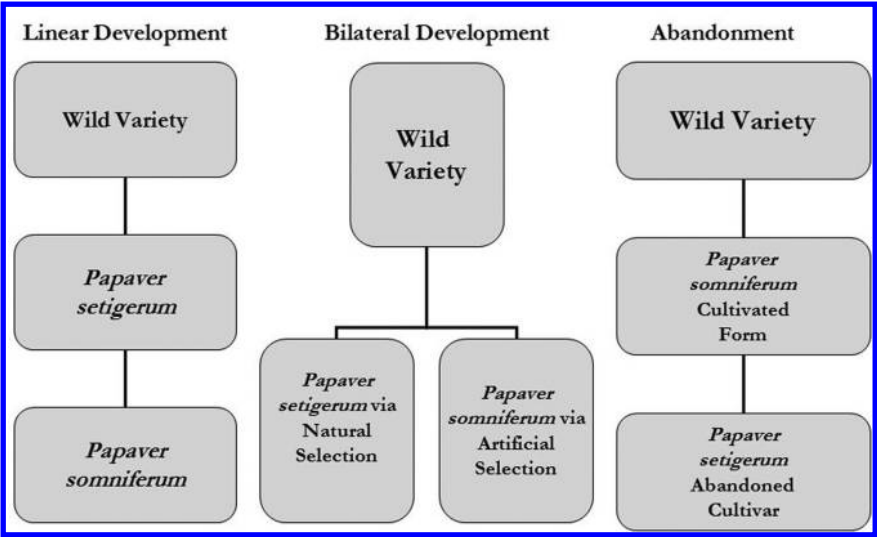


Figure 2. Evolutionary relationships

have and continue to be of great pharmacological interest) belong to four main groups: morphinan, phthalidisoquinoline, benzyltetrahydroisoquinoline, and benzylisoquinoline. The morphinan alkaloids include morphine, codeine, and thebaine. The phthalidisoquinoline alkaloids include noscapine and its derivatives. The benzyltetrahydroisoquinoline alkaloids include laudanosine and laudanine and the aromatic benzylisoquinoline group includes papaverine (Husain and Sharma 1983:29–32, 131; Kapoor 1995:162, 166–167; Petri and Mihalik 1998:50). Alkaloids, so termed for their bitter taste, frequently serve as a defensive mechanism against ingestion by herbivores (Kapoor 1995:206–207; Liscombe et al. 2005:1374–1375; Roberts and Wink 1998:4). Individual alkaloids are synthesized at different stages of plant development and exist in varying quantities and concentrations (Kapoor 1995:104, 200–202; Wink 1998b:287). Since biochemical production is tied to the physiology of a plant, the manner in which alkaloids are “synthesized, altered, or degraded by plant or animal organisms” (Petri and Mihalik 1998:59) are complex processes.

The fact that the opium poppy is a weedy species that rapidly moves into disturbed landscapes presents a number of problems for examining its use archaeologically (Hawkes 1969:18 in Merlin 1984:147; Veselovskaya 1976:19–77 in Merlin 1984:39–42). Since capsules rarely preserve, the majority of botanical

evidence occurs in the form of poppy seeds, which are small in size and structure making their recovery and identification difficult (Merlin 2003:298). Furthermore, in addition to a high concentration of carbohydrates, fats, proteins, vitamins and minerals, oil constitutes forty-five percent of the total seed weight (Addens 1939:43; Bernáth 1998:338; Duke 1973:391 in Merlin 1984:91). Therefore, the opium poppy constitutes a significant subsistence resource and its narcotic use cannot be assumed.

Any investigation of the non-subsistence use of the opium poppy in antiquity must satisfy four conditions: 1) botanical remains must be cultural and contemporaneous with human settlement, 2) specimens must be identified to the species level, 3) human use of the plant must be demonstrated, and 4) the nature of this use must be shown to have been for narcotic purposes.

### *The Opium Poppy in the Archaeological Record*

Archaeological evidence for the prehistoric use of the opium poppy primarily occurs in three geographic regions: Central Europe, the Mediterranean basin, and the Near East (Figure 3). The majority of evidence has been recovered from Central European Neolithic and Bronze Age sites in close proximity to lakes (Merlin 1984:121–122, 128, 136–137, 134–138). There are some forty lakeshore settlement sites located in present-day Switzerland, Austria, Germany, France and Italy (Merlin 1984:111–112). Archaeological evidence for the opium poppy from these sites occurs primarily as preserved seeds. Much of this evidence is vaguely described in the literature with only a small fraction of the total seeds identified as *P. somniferum*. Radiocarbon dates are rare and seldom calibrated (Merlin 1984:26–27; Rudgley 1993:25). There is little that suggests that the opium poppy from these sites was being utilized for narcotic purposes.

The earliest evidence that suggests knowledge of the opium poppy's narcotic properties dates to the mid-sixth millennium B.C. from the underwater site of La Marmotta, on the western coast of Italy. Preserved poppy seeds found in a ritual chamber constitute the earliest evidence for the opium poppy in a sacred context (Kunzig 2002; Merlin 2003:302–303; Neroni 2006). The nature of the plant's use is assumed to be narcotic due to the context; however, the poppy seeds are not associated with the organelles that produce the alkaloid-rich latex (Kapoor 1995:198–200; Nessler 1998:210). Conspicuous evidence for non-subsistence use of the opium poppy comes from a cave site near Albuñol in Spain. A Neo-



**Figure 3.** Geographic Distribution of Opium Evidence (Google Earth, 2008. Europe, Mediterranean Basin, Northern Africa. Mountain View, CA: Google, Inc.)

lithic period burial in La Cueva de los Murciélagos yielded preserved poppy capsules and human hair in woven grass bags (Merlin 1984:173, 2003:303). Gongora (1868:36, 55 in Merlin 1984:160–70) argued that this may represent “the symbol of a dreamful sleep and the image of the dead”. Some social or religious value attributed to the opium poppy is undeniable.

The earliest evidence for opium poppy in the Eastern Mediterranean comes from Pre-Pottery Neolithic C (PPNC) Atlit Yam, an underwater site off the coast of Israel. A structure identified as a well contained a variety of plant and animal remains, including one *Papaver setigerum* seed (Kislev et al. 2004:1301–1305). The presence of a single seed certainly does not constitute evidence for the knowledge and use of the narcotic properties or the cultivation of the opium poppy. The site dates approximately to the eighth millennium B.C., which constitutes the earliest attestable archaeological evidence for opium poppy. In addition,

paleobotanical evidence was recovered from an Early Bronze Age site on the island of Lesbos in the form of two charred poppy seeds. However, the specimens were not identified to the species level. Moreover, the charred state is most likely the result of natural carbonization (Merlin 1984:159–60). On the Anatolian mainland, a single poppy seed was recovered from a vessel from a burned palace at Beycesultan dating to the second millennium B.C. (Merlin 1984:160–161; Merrillies 2003[1979]:122). In all of these cases, the evidence fails to satisfy the four conditions to be considered evidence of a narcotic use of the opium poppy.

Suggestive evidence comes from a handful of sites further south and east. At Deir el-Medineh, Egypt, Merlin (1984:278–279) stated that a single unincised poppy capsule was recovered from a New Kingdom Tomb (Bisset et al. 1994:108; Koschel 1996:160). Such a find may suggest that the plant may have been valuable, but the species was not specified. More convincing evidence originates further east from the Zoroastrian capital of Gonur Depe in Turkmenistan. In a shrine dating to the mid-second millennium B.C., Russian archaeologists recovered remains of *Ephedra* and *P. somniferum*, as well as *Papaver* pollen from an engraved bone tube that purportedly represents a smoking pipe (Merlin 2003:301–302; Sarianidi 1994).

Alleged pipes also have been recovered from potential ritual contexts on Crete and Cyprus. At the Late Minoan site of Gazi, Crete, a tubular base, which has been likened to modern opium pipes from Southwest Asia, was recovered from the floor of a subterranean room associated with charcoal and two terracotta figurines (Merlin 1984:241–247; Merlin 2003:306, 308). The larger of the two figurines, termed by Marinatos as the “Poppy Goddess, Patroness of Healing” (Arnott 2001:268; Kritikos and Papadaki 1967:23–24), has three removable pins, the heads of which are in the shape of opium poppy capsules. Numerous pins with poppy-like heads have been recovered from various parts of the Eastern Mediterranean (Arnott 2001:268–270; Gabra 1956; Merlin 2003:303,306,308; Merrillies 2003[1979]:122,126). Additional suggestive paraphernalia has been recovered from two temples from the Late Bronze Age urban center of Kition, on eastern Cyprus. According to Karageorghis (1976), a slender, tubular artifact made of ivory with traces of burning around the opening in the shaft and a ceramic tubular vase with a Cypro-Minoan sign inscribed on either side were recovered from Temples IV and V, respectively (Karageorghis 2002:107). The ivory artifact was described by Karageorghis (1976) as an opium pipe and the vase as a smoking implement that would have been used with a base like the



**Figure 4.** Base Ring Juglet (Reprinted, Courtesy of the Semitic Museum, Harvard University, Cambridge, MA).

one recovered from Gazi. Although the suggestion is intriguing, the evidence is insufficient to demonstrate opium use.

Much of the evidence suggesting knowledge and use of the opium poppy for narcotic purposes derives from the interpretation of botanical representations on artifacts and structures. Alleged representations of the opium poppy occur in the form of depictions of the plant in scenes with humans and animals, jewelry, statuettes with similar jewelry items, statues with depictions of the plant, pins with poppy capsule heads, and ceramic vessels.

Of particular interest in the latter category are the Base Ring juglets that were produced in Cyprus and traded throughout the Eastern Mediterranean in the first half of the Late Bronze Age (1650–1350 BCE) (Merrillees 1992). The juglets tend to measure between 13 and 17 cm in height and have a ring base. The juglets have a characteristic form and frequently exhibit distinctive decoration (See Figure 4) (Åström 1972:137, 173–174; Bisset et al. 1994:107; Karageorghis 2002:13, 41, 54; Koschel 1996:159; Merlin 1984, 2003; Merrillees 2003[1962]:2–3, 2003[1979] 123–124). Merrillees (2003[1962]) first proposed that, in connection with the high quality of the ware and its wide distribution, the form of the juglets was consistent with the dimensions of an inverted opium poppy capsule and the decoration consistent with the incision method by which the latex is extracted. According to

Kapoor (1995:71–75), the opium poppy capsule is incised with a specialized knife, causing the latex to exude from the cut and resulting in one or more vertical scars on the exterior of the capsule. While evidence for *P. setigerum* or *P. somniferum* is lacking, both species would have grown well in Cyprus in ancient times, just as the former does today (Meikle 1977:78–79). However, in the absence of paleobotanical evidence, the interpretation of botanical representations is a highly subjective endeavor and any acceptance of proposed botanical identification requires corroborating chemical evidence.

### *Chemical Evidence for Opium in Antiquity*

Some chemical analysis has been conducted on artifacts recovered from an Egyptian tomb dating to the XVIIIth Dynasty. Funerary equipment included seven vessels recovered from the sarcophagus which held various oils (Bisset et al. 1994:100). On the basis of colorimetric tests and the physiological responses of frogs and mice to injections of varying amounts of the residue obtained from one vessel, Muzio (1994[1925]:112–114) concluded that the substance was a vegetable oil that contained iron and opium. These results may indicate that the vessel contained some sort of psychoactive substance, but the reactions that Muzio observed were not limited to opium alkaloids and thus do not constitute evidence for opium (Bisset et al. 1994:100).

Bisset et al. (1994) reexamined these vessels with microscopy, various chromatographic methods, as well as the color and physical tests used by Muzio. A problem encountered in the reassessment was the lack of specification regarding which vessels returned which results. Bisset et al. (1994:105–107) asserted that while the same color reactions were observed, additional reactions characteristic of morphine were not observed. Thus, it was concluded that the six vessels that were analyzed did not contain detectable amounts of morphine, codeine, or thebaine.

Additional attempts to identify opium in ancient contexts have largely centered on ceramic containers produced in and transported from Cyprus. Evans (in Merrillees 2003[1989]) reported finding opium and olive oil in a Base Ring sherd from the Institute of Archaeology, London University and opium along with an unidentifiable, degenerate oil in a Base Ring sherd from the Rockefeller Museum in Jerusalem. Despite the inclusion of the description of the analytical techniques utilized (gas-liquid chromatography [GLC], high performance liquid chromatography [HPLC], thin layer chromatography [TLC], and infrared spectroscopy [IR]) the fact that compounds were identified based on lipids rather than alkaloids make it unclear what criteria were employed for determining the

presence of opium (Koschel 1996:162). Perhaps the most comprehensive study thus far was conducted by Koschel and Bisset's research group on an unwashed Base Ring II juglet from New Kingdom Egypt. The vessel contained "a yellowish-brown amorphous resin-like residue mixed with quartz sand grains" (Koschel 1996:161). Analysis by TLC, GC, and mass spectrometry (MS), showed approximately 0.1 percent of opium alkaloids in the sandy residue. Analysis by radioimmunoassay (RIA) showed 0.05 percent of morphine. The percent of concentrations are quite significant because they indicate that the opium likely was dissolved in some form of liquid, thus constituting conclusive chemical evidence for opium in the juglet (Koschel 1996:161).

Belgiorno (2004:27) suggested that numerous botanicals, including opium, were identified at the Middle Bronze Age site of Pyrgos-Mavroraki in southern Cyprus. However, the analytical data for the opium identification are lacking beyond a brief mention in a 2004 publication (Lentini 2004:47, 69). All identifications were based on colorimetric reactions, which can be useful for preliminary assessments but, by modern standards, require further corroboration. More recently, Rebecca Stacey (2008) through personal communication revealed that the original contents of two sealed Base Ring juglets at the British Museum were analyzed and preliminary results suggested the presence of papaverine. In a later paper and personal communication with Collard (2010; 2008), he stated that Stacey's and Koschel's results indicated a relationship between the Base Ring juglets and opium. However, like Merrillees, Collard oversimplifies the association and its implications.

To date, the only published study to explicitly demonstrate the presence of opium alkaloids in a Base Ring juglet was conducted by Koschel (1996). Furthermore, a persistent problem in evaluating this opium hypothesis is the analysis of museum specimens that lack provenience, making larger consideration of social use untenable. Collard<sup>1</sup> has attempted to address this by collecting samples *in situ* from active excavations.

There are, however, methodological challenges in identifying opium alkaloids in ancient residues. The primary aim of this study is understanding the diachronic behavior of opium compounds in an effort to assess the feasibility of identifying opium in archaeological contexts, as well as determining which compounds are most likely to be preserved.

### *Experimental Materials and Procedures*

The purpose of this study was to simulate and monitor the transformation and degradation processes of opium alkaloids. The processes identified during the

course of this study represent an accelerated form of the decomposition of opium that occurs in archaeological contexts. Such an experimental approach is essential in determining whether constituent alkaloids are detectable, in assessing the relative stability of these biochemicals, and in identifying by-products of degradation pathways which may not be identifiable in fresh opium samples. Such data may aid in the identification of opium in archaeological contexts.

We began our experimental approach by preparing a standard solution that consisted of scientific-grade opium and ethanol. In order to simulate accelerated chemical degradation, two aliquots of the standard were sealed in glass flasks. One sample was placed in a laboratory oven set at 70°C; the other was placed under an ultraviolet lamp (250 nm). The flasks were removed after one week, two months, and four months, at which time a sample of each was analyzed by gas chromatography/mass spectrometry (GC/MS). Organic compounds were extracted using a reflux apparatus with a mixture of ethanol and methanol (25 mL, 1:1, v/v). Following volume reduction under a controlled stream of nitrogen gas, samples were analyzed using a Hewlett Packard 6890 gas chromatograph in tandem with a 5972A selective mass detector.

The GC/MS is equipped with a 1  $\mu$ L auto-injector and fitted with an HP-5 capillary column measuring 30 m in length, 250  $\mu$ m in diameter with 5 percent phenylmethylsiloxane and a film thickness of 0.25  $\mu$ m. Initial temperature was held at 150°C for 1 minute then ramped to 280°C at 15°C/minute and held for 3 minutes, with a total run time of 12.67 minutes. There was a splitless interface to the quadrupole mass selective detector with a 2 minute solvent (acetone) delay and a mass range from 50 to 500.

Three opium reference spectra were obtained. The first, illustrated in Figure 5a, was obtained from the opium-ethanol solution prepared for the aging study. The second spectrum (see Figure 5b) was obtained from a sample of scientific-grade opium extracted with heptane and injected directly into the GC. Lastly, a sample of opium was burned, extracted using the same extraction procedure described for the aging samples, and injected into the GC (see Figure 5c).

## *Results and Discussion*

Admittedly, opium and the constituent alkaloids targeted by this study have long been the subject of chemical, pharmacological, botanical and historical examination (Dewick 2002; Galat 1950; Hesse 1981; Husain and Sharma 1983; Trost and Tang 2002; Veselovskaya 1976 in Merlin 1984). It is also acknowledged that

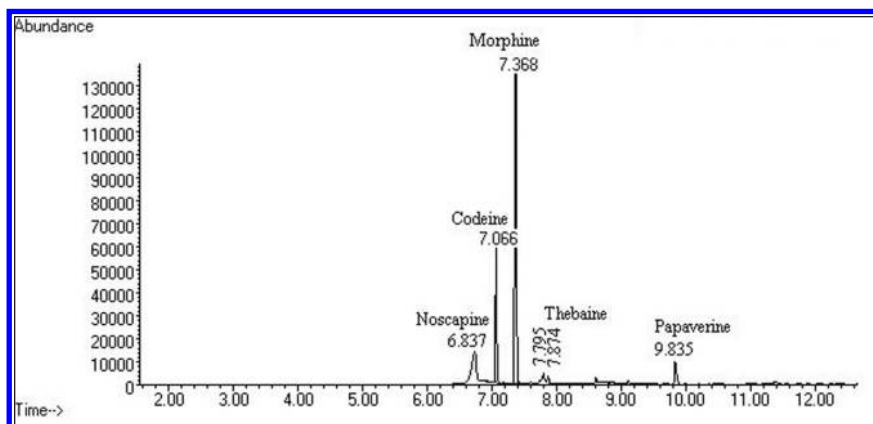


Figure 5a. Opium in Ethanol Reference Spectrum.

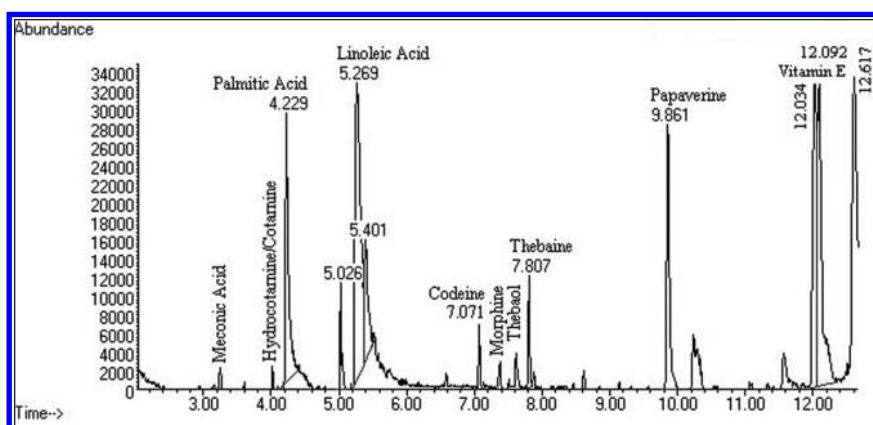


Figure 5b. Opium in Heptane Reference Spectrum.

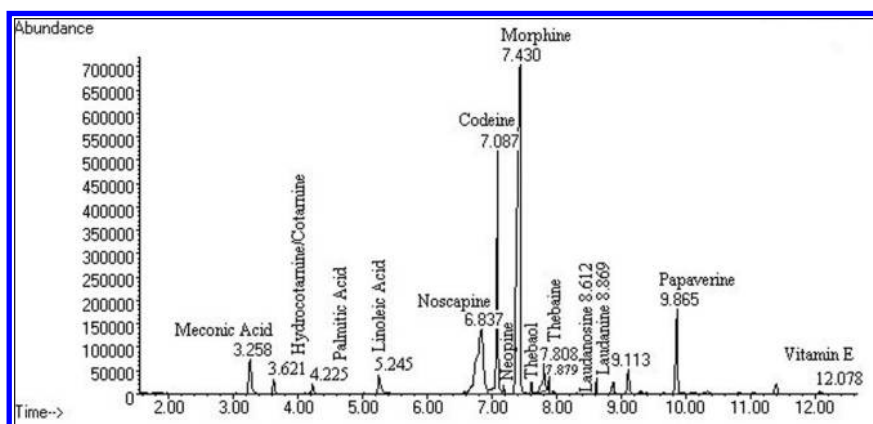


Figure 5c. Burned Opium Reference Spectrum.

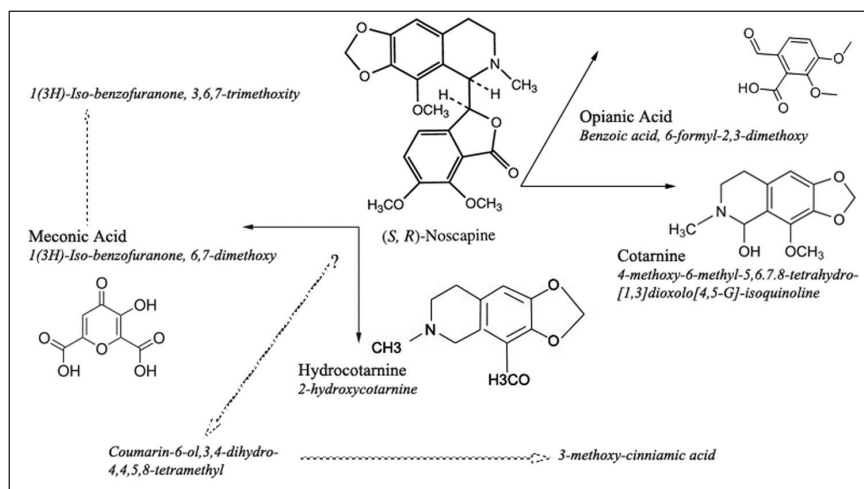


**Figure 6.** Degradation Pathway of Noscapine.

the formation pathways of these alkaloids have long been known. The focus of such studies has, however, been economic in nature. The experimental study discussed here utilizes previous chemical research to illuminate the diachronic behavior and stability of these biochemicals, which have not previously been investigated. The results of this study will focus on the alkaloids that produce the greatest physiological effects and will be discussed in three sections: 1) the phthalidisoquinoline alkaloids (noscapine, cotarnine, opianic acid, hydrocotarnine and meconic acid); 2) the benzyltetrahydroisoquinoline and aromatic benzylisoquinoline alkaloids (papaverine, laudanosine, and laudanine); and 3) the morphinan alkaloids (morphine, codeine, and thebaine).

## Phthalidisoquinoline Alkaloids

The phthalidisoquinoline alkaloid, noscapine, degraded rapidly into four constituent alkaloids that survived the aging experiment. These chemical by-products showed to survive thermal and light-induced chemical degradation and therefore should be targeted in future attempts to identify opium in archaeological contexts.

Noscapine<sup>2</sup> has four decomposition pathways which have been demonstrated experimentally and are illustrated in Figure 6. The solid line arrows indicate

known dissociation pathways while dotted line arrows indicate further dissociations identified during the course of this experimental procedure. The results of the first dissociation are cotarnine<sup>3</sup> and opianic acid.<sup>4</sup> The second dissociation results in hydrocotarnine<sup>5</sup> and meconic acid<sup>6</sup> (Stewart 1920:138–142). Overall, noscapine did not survive the aging experiments, which indicates that the compound decomposes rapidly. Figures 7 and 8 illustrate the spectra obtained after each round of heating and UV irradiation, respectively.

After one week of degradation, peaks were observed at retention times between 6.693 and 6.829 minutes. While there were no mass spectra matches for noscapine, the retention time range is consistent with those observed for the compound in the reference spectra. After two months, peaks (and spectra) were recorded for meconic acid, opianic acid, hydrocotarnine and cotarnine. Peaks with retention times between 3.621 and 3.651 minutes had spectra matches for both hydrocotarnine and cotarnine. This suggests that it may be difficult to differentiate between these two alkaloids. For this reason, the compound matches for this peak will be referred to as (hydro)cotarnine hereafter.

Following two months of both types of degradation, there was a substantial increase in the abundance of both meconic acid and (hydro)cotarnine. In the UV sample, the abundance of opianic acid was slightly less than that of noscapine in the reference spectra. Such abundant fluctuations are likely related to instrumental and sampling variation, as well as the further dissociation of these compounds. Regarding the identification of compounds that are the result of greater degradation, a coumarin compound<sup>7</sup> occurring within the range of (hydro)cotarnine should be noted. According to Bowles (2003:106–8), coumarins are plant compounds that have a cinnamic acid<sup>8</sup> skeleton, have a vanilla odor, and serve a variety of biological functions. There were no peaks observed at this retention time in the initial standard or after the first round of heating and UV irradiation. After the second and third rounds of heating, both the coumarin and the respective cinnamic acid skeleton were identified. In the second round of UV irradiation, (hydro)cotarnine, the coumarin, and the cinnamic acid skeleton were observed, in addition to noscapine, albeit at a very low quality. After four months of UV irradiation, only (hydro)cotarnine is identified. The overall variability in this area of the chromatogram may indicate that the coumarin and cinnamic compounds represent additional degradation products of phthalidisoquinoline alkaloids or may simply relate to the solubility of noscapine. Further investigation is needed to confirm this suggestion.

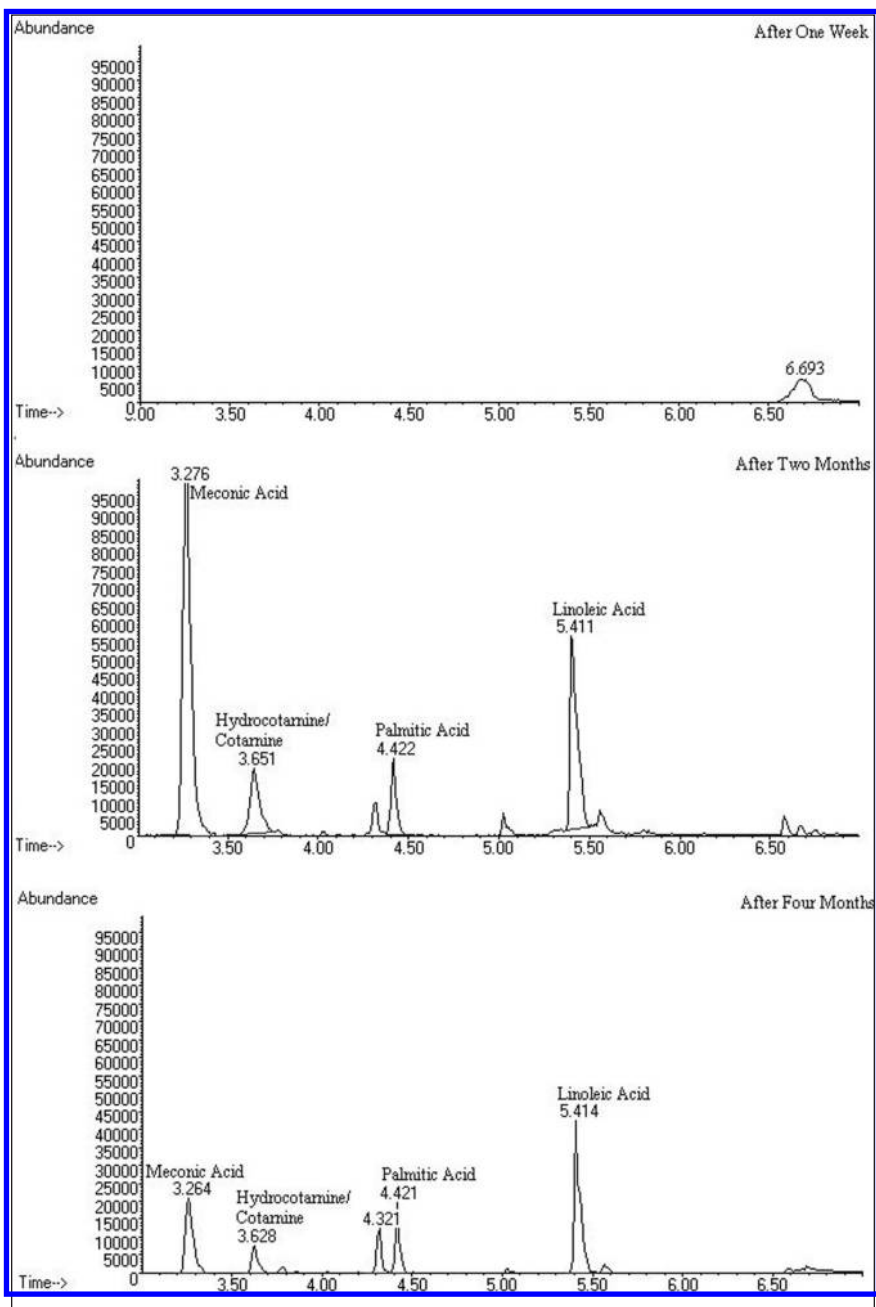


Figure 7. Opium in Ethanol Aged by Heating in Noscapine Region.

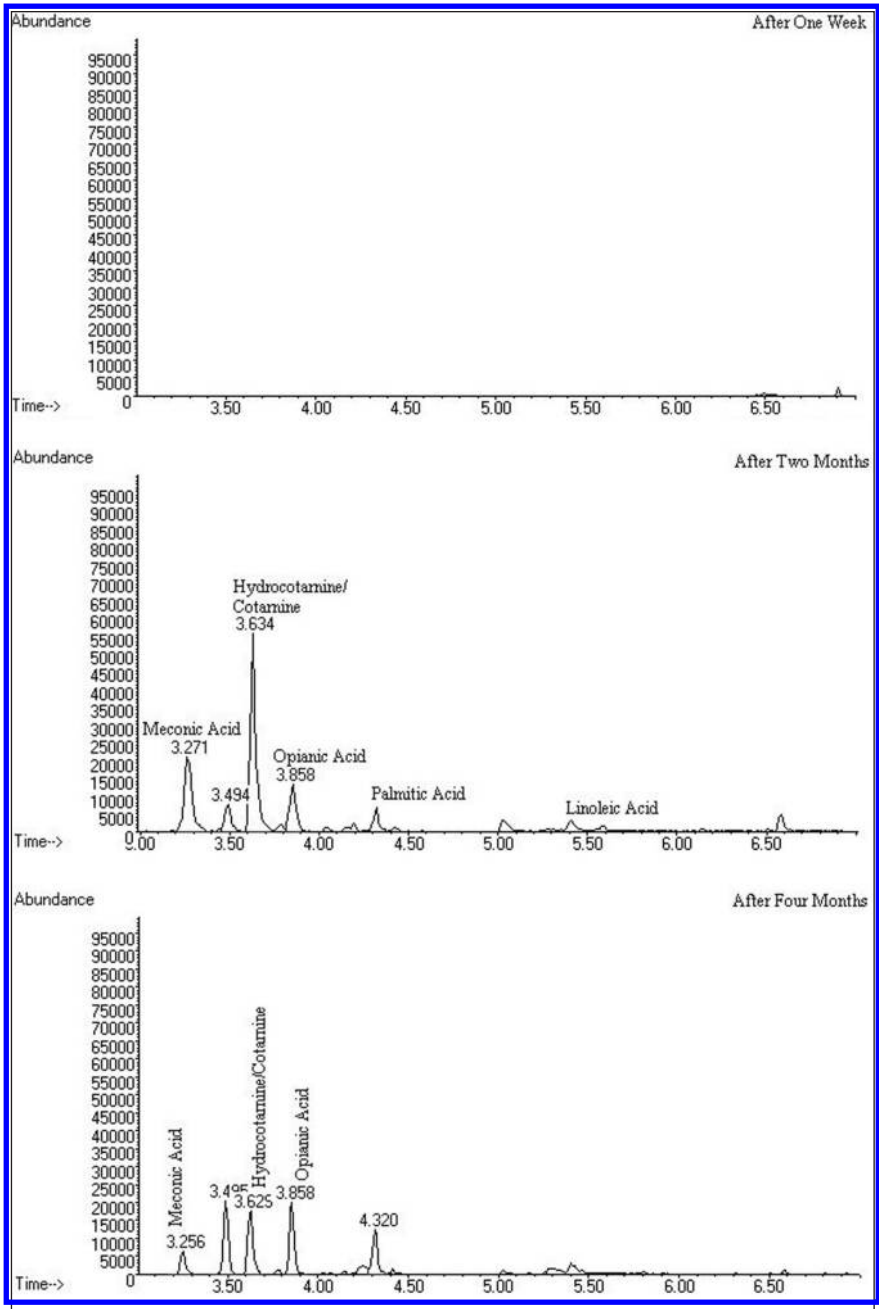


Figure 8. Opium in Ethanol Aged by UV Light in Noscapine Region.

Similar observations were made after the final round of degradation for the remaining decomposition products. After four months, both meconic acid and (hydro)cotarnine decreased to a quarter of the abundances recorded after the second round of degradation. Opianic acid was slightly greater than (hydro)cotarnine in the UV sample, but appeared only as a small peak in the heated sample that was only identified by retention time. The difference in the behavior of these alkaloids under the different conditions has two major implications. First, opianic acid likely degrades due to photo-oxidation, while (hydro)cotarnine likely results from photo-oxidation and thermally-induced chemical degradation.

### **Benzyltetrahydroisoquinoline and Benzylisoquinoline Alkaloids**

Studies of the benzylisoquinoline alkaloid, papaverine<sup>9</sup>, have demonstrated the complexity of its synthesis and degradation. This became evident during the course of the experiment in fluctuations in the abundances of papaverine, laudanosine, and laudanine. While papaverine remained stable under most conditions, the overlapping biosynthetic pathways made assessing the diachronic behavior of these alkaloids difficult. Figure 9 illustrates these overlapping pathways.

After one week of heating, there was only a slight reduction in the abundance of papaverine. After two months, the peak tripled with an abundance far above that of morphine or codeine, while retaining a very high quality (99 percent). After four months, however, the compound was not identified. Following two months of UV irradiation, there was a substantial increase in abundance, which is reduced by half after four months. Despite this reduction at the end of the experiment, the abundance of papaverine remains nearly three times that of morphine or codeine (see Figures 10 and 11).

The fluctuations in abundances appear to be rather significant, but are likely a product of the biosynthetic pathway. Of particular interest is the relationship between papaverine and laudanosine<sup>10</sup>. In addition to being an important precursor to papaverine, laudanosine also decomposes into laudanine<sup>11</sup> (Hosztafi 1998; Piotrowska et al. 2002; Stewart 1920:138–142). These compounds were identified in the sample of burned opium at retention times of 8.612 and 8.869 minutes, respectively. Elsewhere their presence was determined by comparison of these retention times. Papaverine tends to preserve well under most conditions, while laudanosine and laudanine tend to preserve better in thermally-induced conditions. The reason for the latter is associated with the relative degree of decomposition of papaverine.

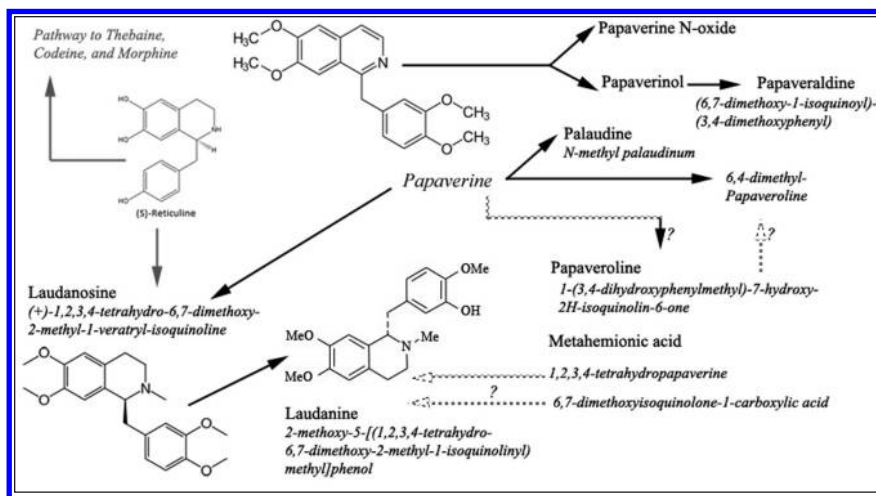


**Figure 9. Degradation Pathway of Papaverine.**

## Morphinan Alkaloids

The final group of alkaloids that will be discussed are the biochemicals related to morphine<sup>12</sup> (Petri and Mihalik 1998:50). The most noteworthy observation was that morphine, the most abundant opium alkaloid, degraded rapidly. Codeine's decomposition was accelerated under UV light, while thebaine proved to remain stable under most conditions. Experimental results for this alkaloid group are highly significant in that most archaeological studies have targeted morphine, the most abundant alkaloid found in fresh opium. This is demonstrated experimentally in that morphine appears as the largest peak in the opium standard and the burned opium spectra. Morphine is represented as a smaller peak in the opium sample extracted with heptane and is a result of differential solubility of the compound. Throughout the experiment, the retention time for morphine ranged from 7.359 to 7.438 minutes and these identifications were made both by mass spectra matches and by retention time comparisons.

After one week of heating, the abundance of morphine decreased to less than a third of the original amount observed in the opium standard, but was still the largest peak in the chromatogram (see Figure 12). The degree of initial decomposition was even greater after the first round of UV irradiation (see Figure 13). Following the second round of heating, the abundance of morphine reduced drastically, being identified only by retention time. After four months of heating, the

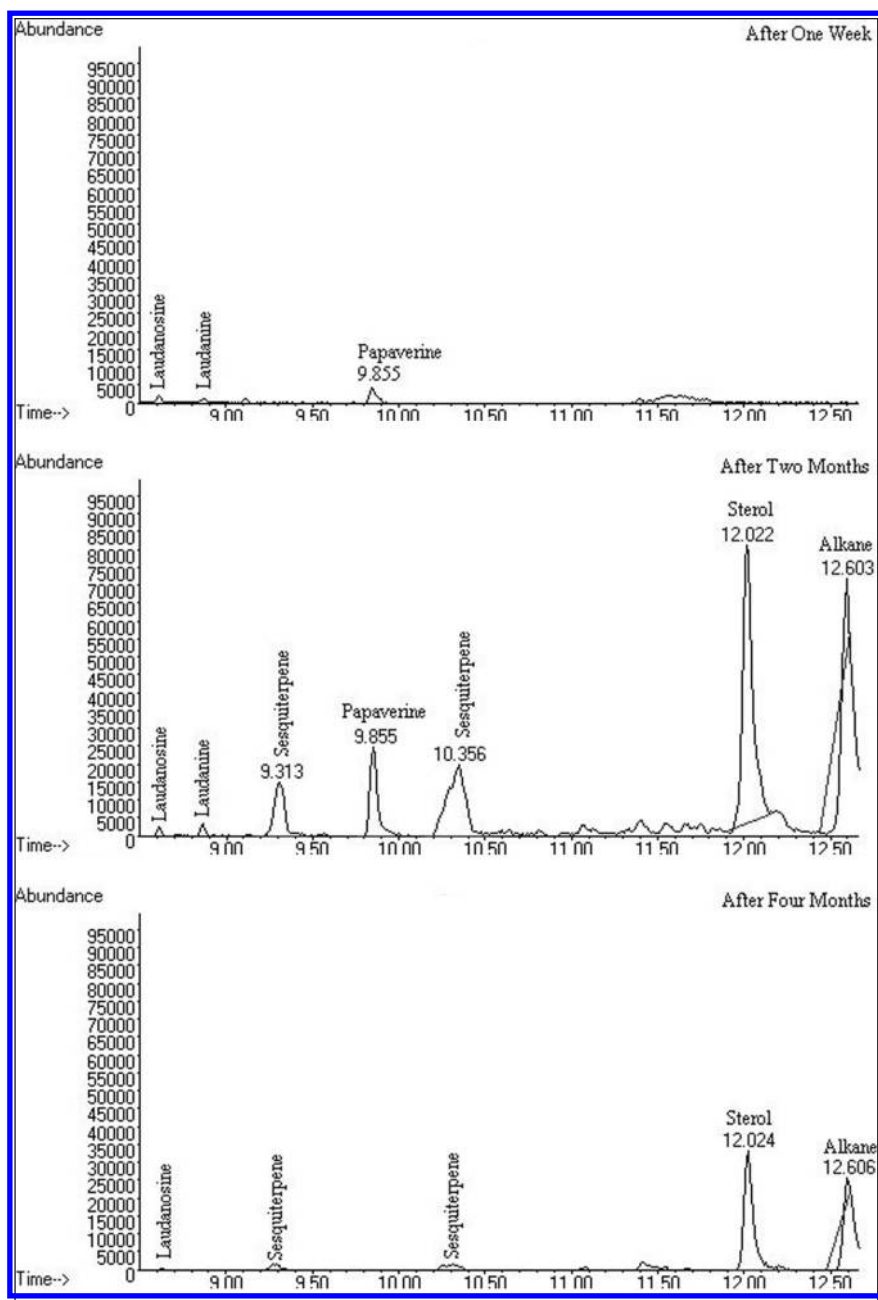


Figure 10. Opium in Ethanol Aged by Heating in Papaverine Region.

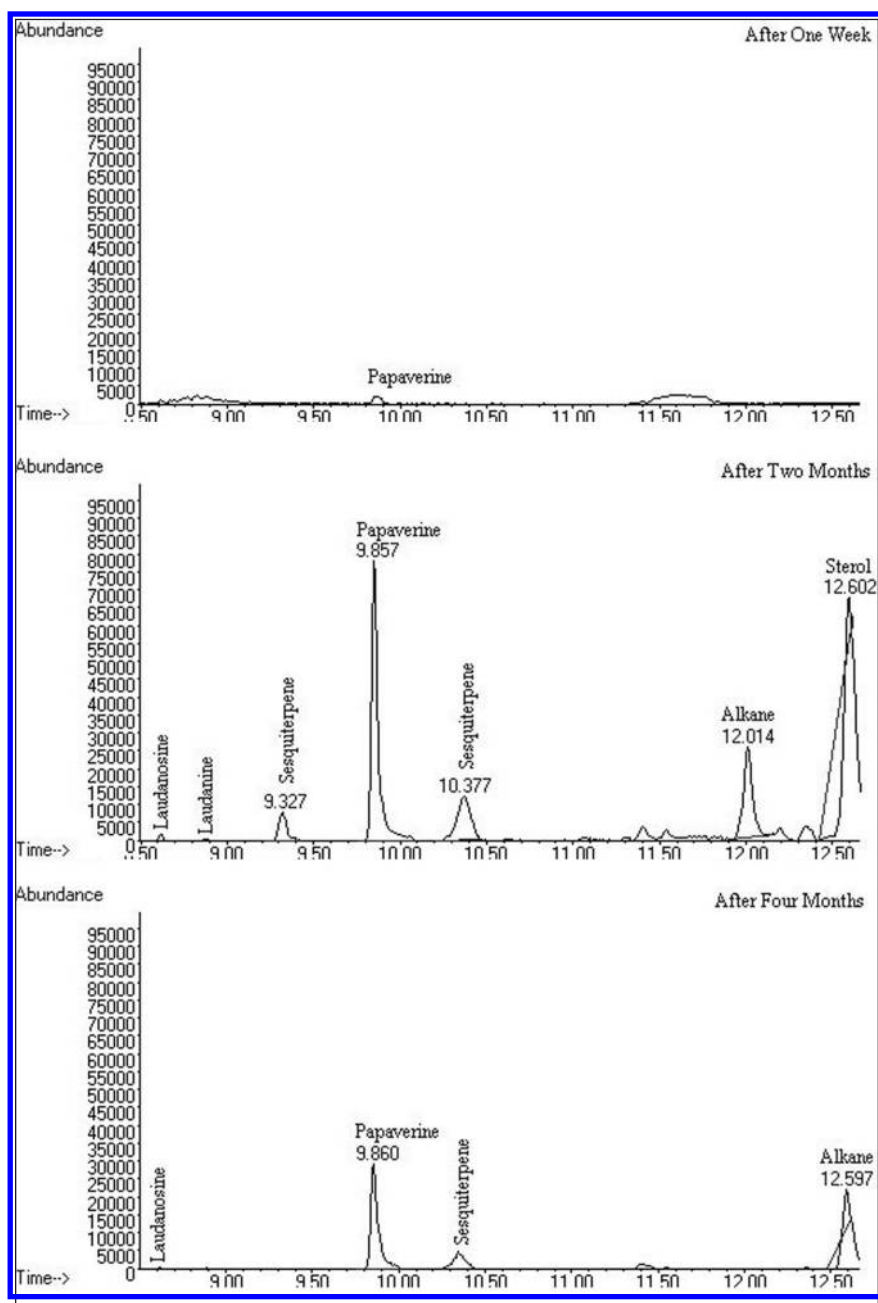


Figure 11. Opium in Ethanol Aged by UV Light in Papaverine Region.

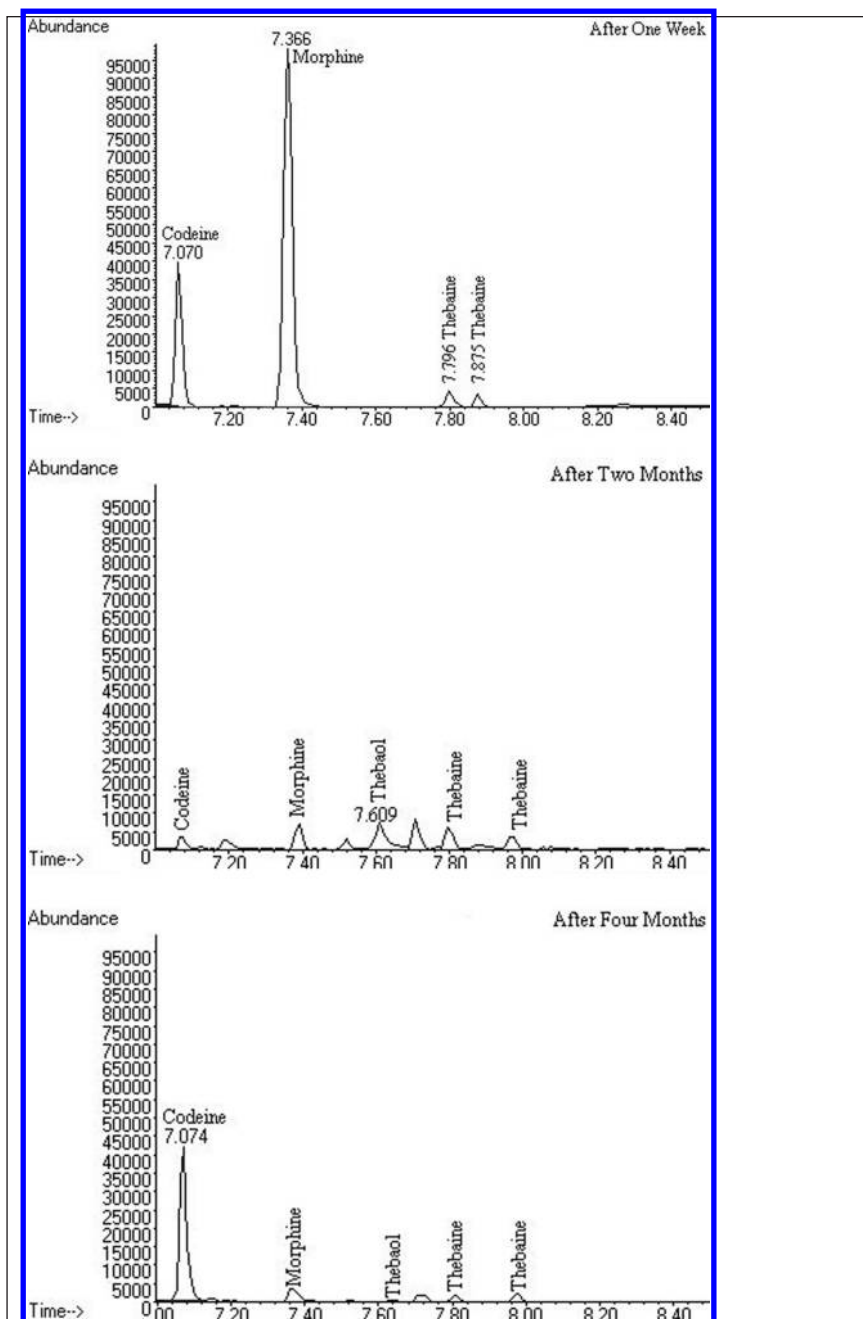


Figure 12. Opium in Ethanol Aged by Heating in Morphine Region.

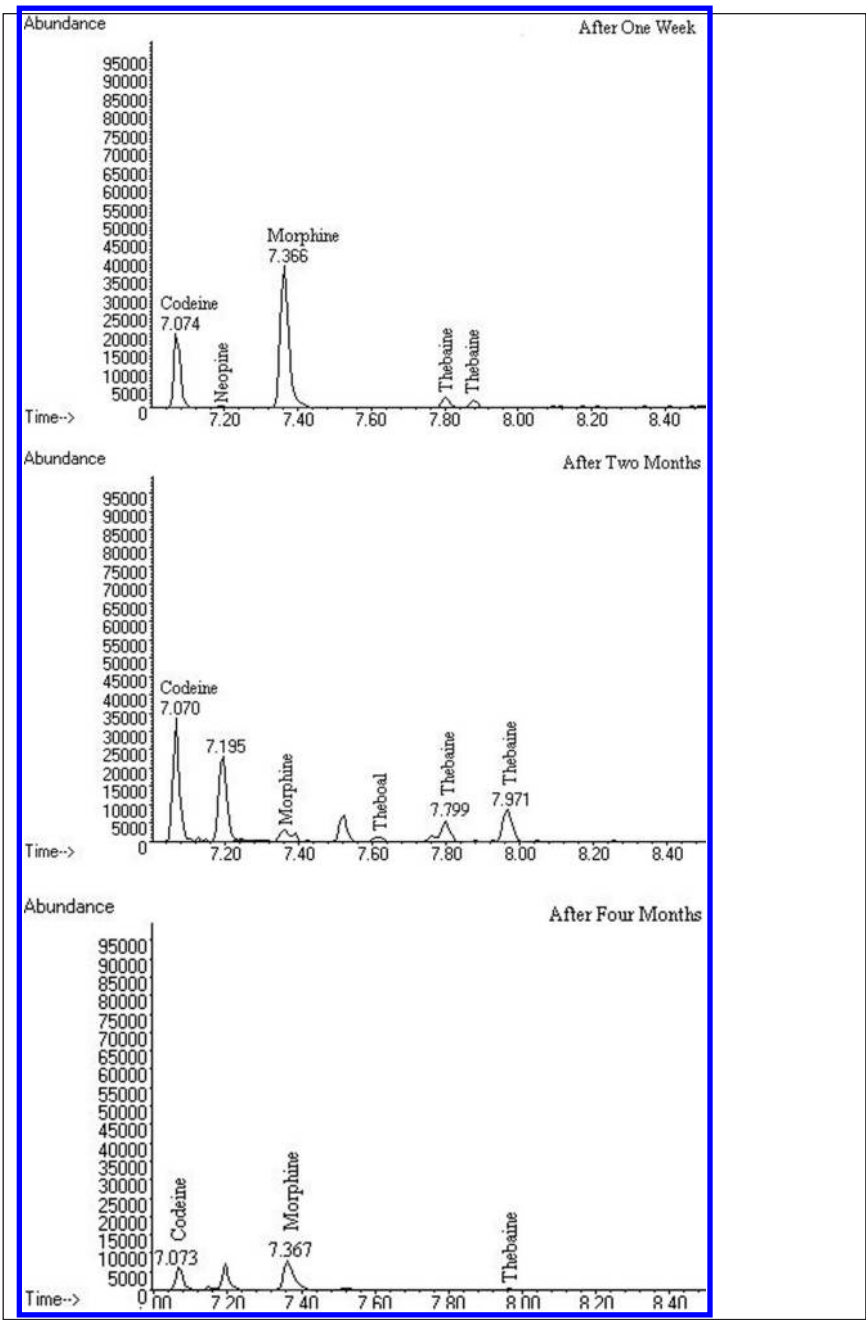


Figure 13. Opium in Ethanol Aged by UV Light in Morphine Region.

amount of morphine reduced even further and again was identified only by retention time. A similar trend of abundance reduction was observed after two months of UV irradiation. However, after four months, morphine's abundance increased slightly and was identifiable with a rather high quality (94 percent).

These observations are significant for three main reasons. First and most importantly is that while morphine is the most abundant alkaloid in fresh opium, it degrades rapidly. Second, while thermal- and photo-oxidation had the same end result, namely that the same degree of degradation occurred, the initial degradation was greatest in thermal oxidation. The final point is demonstrated in Figure 13, which illustrates the multiple routes of the synthesis and degradation of the morphinan alkaloids. The inherent complexity within this biosynthetic pathway and the fluctuations in morphine's abundance indicates that the behavior of this important compound must be understood in conjunction with the other alkaloids involved in the pathway.

One of these compounds is thebaine<sup>13</sup>, which is a precursor of both morphine and codeine<sup>14</sup> as illustrated in Figure 13 (Horn et al. 1978:1895–1898; Preininger 1986:23; Pšenak 1998:105–110; Stewart 1920:164–165). In all reference and degradation spectra, thebaine occurs as either one or two peaks with retention times that range from 7.795 to 7.808 minutes and 7.874 to 7.877 minutes, respectively. Whether the compound is identified by mass spectra match or simply by retention time, thebaine has consistently small peaks. Despite this fact, thebaine does appear to be relative stable, especially under conditions of thermal oxidation. This is particularly true for thebaine's first and stronger peak. However, after two months of photo-oxidation, thebaine does dissociate in some degree into thebaol<sup>15</sup> (Theuns et al. 1985). After four months, all three peaks almost completely disappear. The fluctuations in the abundance of thebaine and thebaol are likely related to the relative abundance of codeine.

Codeine occurs in all reference and degradation spectra between 7.066 and 7.087 minutes. As indicated in Figure 14, codeine is the primary precursor to morphine, which makes its measured abundance directly related to that of the latter. After one week of heating, the alkaloid's abundance reduced by nearly half. After two months, it reduced to only a small peak that was identified only by retention time. However, after four months of heating, the abundance of codeine returned to the level present after the first round of heating. This increase is consistent with the reduction observed for thebaine. Similar to the behavior of morphine, codeine degraded more substantially by photo-oxidation after one week

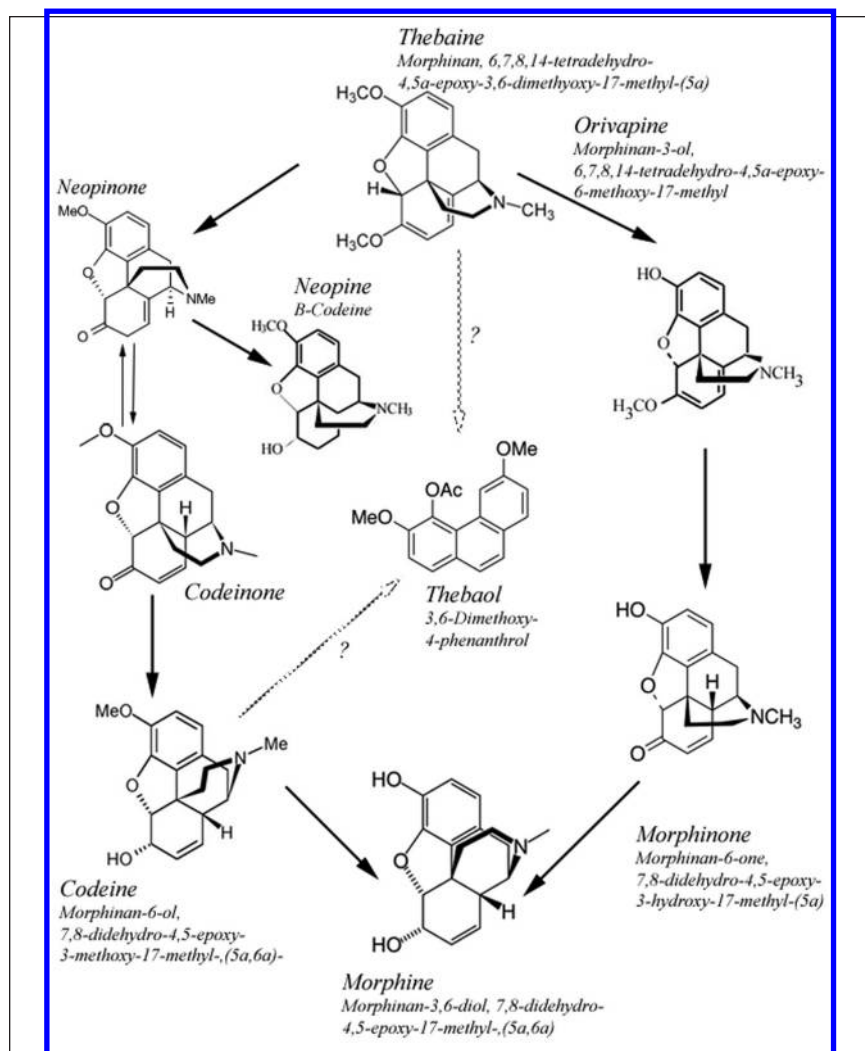


Figure 14. Degradation Pathway of Morphine.

of irradiation. As observed with morphine's behavior, codeine is greatly reduced by photo-oxidation after one week. The increase after two months and decrease after four months is consistent with the fluctuations observed for morphine. Similar kinds of fluctuations and reductions were observed by Oustric-Mendes et al. (1997) in their investigation of morphine's stability.

In sum, the described experimental study assessed the relative stability of

opium alkaloids with the greatest physiological effects and identified chemical constituents found in opium that are most likely to preserve in archaeological contexts. Of the morphinan alkaloids, morphine was determined to be least stable and thebaine most consistently stable. In the phthalidisoquinoline group, hydrocotarnine, meconic acid, and opianic acid are the chemically stable degradation products of noscapine. And lastly, the benzyloisoquinoline alkaloid, papaverine, proved to be stable under most conditions, but the complexity of its biosynthetic pathway may result in abundance fluctuations. While this was demonstrated to primarily apply to potential identifications of the benzyloisoquinoline and benzyltetrahydroisoquinoline alkaloids, it should be noted that the measured abundances of any one of the discussed alkaloids is directly related to the abundances of its precursors and decomposition products.

## *Conclusions*

The aim of this study was to generate a diachronic model of the behavior of opium alkaloids. Applying these data to the investigation of the human exploitation of the opium poppy for narcotic purposes creates a baseline for identifying opium residues in archaeological contexts. The most significant result observed is the fact that morphine, the most abundant alkaloid in opium, does not preserve well. This conclusion is of great consequence to the chemical investigation of ancient opium residues in that the majority of such studies have focused on the identification of morphine. Thus, the results of this degradation study suggest that it would not be surprising if morphine was not identified. This information, then, allows for the construction of an analytical program that targets the alkaloids and dissociation products that are most likely to preserve in archaeological residues. Further results suggest that papaverine, thebaine, and the dissociation products of noscapine should be targeted in future analyses.

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## Notes

1. Collard, David, e-mail message to primary author, October 19, 2008.
2. (3S)-6,7-Dimethoxy-3-[(5R)-5,6,7,8-tetrahydro-4-methoxy-6-methyl-1,3-dioxolo(4,5g)isoquinolin-5-yl]-1(3H)-isobenzofuranone
3. 4-methoxy-6-methyl-5,6,7,8-tetrahydro-[1,3]dioxolo[4,5-g]isoquinoline
4. 6-formyl- 2,3-dimethoxybenzoic acid
5. 2-hydroxycotarnine
6. 1(3H)-Isobenzofuranone, 6,7-dimethoxy
7. Coumarin-6-ol,3,4-dihydro-4,4,5,8-tetramethyl
8. 3-methoxycinnamic acid
9. 1-(3,4-dimethoxybenzyl)-6,7-dimethoxyisoquinoline
10. (+)-1,2,3,4-tetrahydro-6,7-dimethoxy-2-methyl-1-veratryl-isoquinoline
11. 2-methoxy-5-[(1,2,3,4-tetrahydro-6,7-dimethoxy-2-methyl-1-isoquinoyl)methyl]phenol
12. Morphinan-3,6-diol,7,8-didehydro-4,5-epoxy-17-methyl-,(5 $\alpha$ ,6 $\alpha$ )
13. 6,7,8,14-tetradehydro-4,5 $\alpha$ -epoxy-3,6-dimethoxy-17-methyl-,(5 $\alpha$ )
14. Morphinan-6-ol, 7,8-didehydro-4,5-epoxy-3-methoxy-17-methyl-,(5 $\alpha$ ,6 $\alpha$ )
15. 3,6-Dimethoxy-4-phenanthrol

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