

# Historical and Comparative Perspective of *Set & Setting*: the case of opium in the Early Modern period

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*Abstract:* This article explores the historical and comparative dimensions of the “Set and Setting” model by examining the case of opium use during the Early Modern period. Introduced in the 1960s, the Set and Setting model posits that drug effects are shaped not only by their pharmacological properties but also by the user’s mindset and socio-environmental context. While modern research has embraced this concept to analyze psychedelics and other substances, this study applies it to historical contexts to shed light on variations in drug use and effects across cultures. The article focuses on opium, a psychoactive substance with profound medical and cultural significance, and investigates its dual perception as a medicine and intoxicant. By analyzing accounts from Early Modern physicians and travelers, the study highlights how cultural narratives, environmental factors, and individual dispositions influenced interpretations of opium’s effects, particularly its supposed role as a “war drug” for Middle Eastern populations. The article also traces the evolving understanding of addiction and tolerance, emphasizing the early recognition of non-pharmacological factors in shaping drug experiences. Drawing parallels to contemporary issues such as the opioid crisis, the article underscores the enduring relevance of the Set and Setting framework in understanding the socio-cultural and psychological dimensions of substance use. By integrating historical perspectives with modern insights, the study advocates for a nuanced approach to drug policy, harm reduction, and the regulation of psychoactive substances.

*Keywords:* set and setting, opium, Early Modern Period, drug effects, addiction and tolerance

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The moderate Dose in ordinary Use, to produce the following Effects,  
is from one to three Grains, (more or less) according to the  
Circumstance, Condition, Case, Constitution, Age, &c  
of the Person who takes it.  
(John Jones, *The mysteries of opium reveal’d*, London 1700, p.19)*

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## 1. *Introduction*

The extent to which the effects of psychoactive drugs are fixed and predictable or shaped by social and cultural factors has been debated extensively over the past century, yet it has still not been answered in full. We know how the effects of drugs could vary significantly between users across societies and cultures, but we still don't know exactly how and why that happens. One reason for this lack of information lies in a point many researchers have emphasized for years: "Drug issues are highly political" (Raven, 1997; Burke-Shyne *et al.*, 2017). We already know how prohibitionist policies towards drugs in the second half of the twentieth century hindered scientific research on their effects by imposing legal barriers that limited access to these substances for study (Nutt, 2015). Among the various theories that have attempted to elucidate the variance in the impact of identical psychoactive substances, my attention is drawn to the phenomenon known as *Set & Setting*. This particular psycho-social approach emerged in the 1960' in the field of psychedelic drug research and showed the importance of the interaction between the medicaments, the individual biology and the socio-cultural background of the consumer (Hartogsohn, 2017). In other words, drug researchers claimed that the effects of psychoactive drugs are dependent in large part upon 'set', the personality, preparation, expectation, and intention of the person having the experience, and 'setting', the physical, social, and cultural environment in which the experience takes place. Yet by the 1970s, following the abandonment of psychedelic drug research, the concept of *set and setting* almost disappeared from the literature. In 1984, however, this concept reemerged in the work of psychiatrist Norman Zinberg (1922-1989), who conducted extensive research on the role of set and setting in shaping drug effects not only with psychedelics, but also with drugs such as alcohol, cocaine, and heroin (Zinberg, 1986). In recent years, scientific research on psychedelics has experienced a significant resurgence, driven by promising findings regarding their potential therapeutic applications for mental health disorders. Consequently, researchers have acknowledged and integrated this theory into research protocols as an essential tool for accurately assessing the therapeutic potential and risks associated with these substances (Dalgarno and Shewan, 2015). Also, it is now widely recognized that the concept of set and setting influences the effects of all drugs, not solely those classified as psychedelics, highlighting the complex interplay between individual mindset, environmental context, and pharmacological action in shaping drug experiences. Given these premises, it is unsurprising that throughout history, the unpredictability of the effects of psychoactive substances has posed significant challenges to both medical professionals and policymakers. This uncertainty is compound-

ed by the complex interplay of individual physiological responses, sociocultural factors, and the evolving nature of substance composition and use patterns. Consequently, attempts to regulate and understand these substances have often resulted in unforeseen consequences, highlighting the persistent difficulty in anticipating their full impact on public health and society.

In this context, analyzing historical reports of variations in drug effects and acknowledging the influence of *set and setting* are crucial for contemporary and future approaches to drug policy. History could indeed provide an interesting benchmark to understand how substances interact with human behaviour and societal norms, thus enabling the development of more effective strategies for harm reduction, therapeutic interventions, and regulatory frameworks that are responsive to the diverse and dynamic landscape of psychoactive substance use. Until recent years, the politics of prohibition have plagued the history of alcohol and drugs not only in discouraging research in this field, but also in providing a fallacious cultural context for the analysis of the consumption of mind-altering drugs throughout history. As a result, following the pattern established by politicians and lawmakers, historians believed for a long time that the effect of drugs depended only on their intrinsic chemical and pharmacological properties (Africa, 1961). Also, the idea of “set and setting” seems to challenge a fundamental pharmacological principle, which posits that drugs produce relatively uniform effects across users. By consequence, historians have been reluctant to apply this concept to key historical questions, such as why evidence of drug addiction in Europe appears only from the eighteenth century onward.

While sociological and anthropological studies of drug action have long emphasized the sociocultural dimensions of “set and setting”, applying this framework to historical analysis now offers potential explanations for various unresolved issues in the history of drugs. For example, Paolo Nencini utilized this model to investigate the absence of recreational opium and other intoxicant use in the Ancient world, and Benjamin Breen applied it to explore why certain drugs swiftly became global consumer commodities in Early Modern trade, whereas others remained limited to regional market (Nencini, 2004; Breen, 2022). In this article, I would like to show an example on how historical and comparative research on the *set and setting* in the Early Modern period could be quite useful to understand better both psychoactive drug use in the past and contemporary issues on alcohol and drugs.

Nowadays, Early Modern physicians’ hopes and concerns related to the use of opiates in medicine, looks more interesting than ever before. Since the isolation of morphine alkaloid from the opium poppy in 1805, analgesic medicaments based on opium poppy have been massively used and are by far the most effective analgesic drugs available in the medical marketplace. This

category of medications, however, has contributed to the ongoing “Opioid crisis”, particularly in North America. This includes natural derivatives of the opium poppy, such as codeine and morphine, as well as semi-synthetic opioids like oxycodone and hydrocodone, and synthetic opioids such as methadone and fentanyl. The crisis highlights how contemporary medicine has yet to fully harness the remarkable analgesic properties of the opium poppy in a safe and controlled manner (Kevin, 2017; The Lancet, 2022). Since 1996, when pharmaceutical company Purdue Pharma introduced OxyContin promoting it as a safe and easy to use painkiller, the deaths and abuses related to opioids consumption has risen dramatically. In 2023 the United States National Centre for Drug Abuse Statistics lists that 72% of the 96,700 deaths from drug overdoses are caused by opioids and that over 10 million people misuse opioids in a year (Dowell *et al.*, 2024; Knopf, 2024). Today, in addition to the tragic fatalities resulting from opioid abuse, numerous social issues have emerged, including a rise in crimes associated with the procurement of these substances (Qiushi *et al.*, 2022). These problems highlight the complex interplay between addiction and societal stability, underscoring the urgent need for comprehensive strategies to address the opioid crisis beyond mere medical intervention (Mohammad *et al.*, 2022).

The current opioid crisis can arguably be understood as a phenomenon closely tied to factors related to both set and setting (Friedman *et al.*, 2020). On the one hand, set encompasses issues such as chronic pain, mental health struggles, dependency, and poverty, while, on the other hand, setting involves systemic challenges, including the dysfunctions of the healthcare system and the significant socio-economic inequalities prevalent in the United States. Analyzing this crisis may benefit from a deeper exploration of the historical dynamics of set and setting as they pertain to opium use in the Early Modern period, offering insights into how societal and contextual factors have long influenced patterns of drug consumption and their outcomes.

## 2. *Case study: the effect of opium in the Early Modern period*

The role of opium in the Early Modern period represents a particularly interesting case study, as it became the subject of reflection and discussion that other “drugs” had not previously received. Many of the most renowned figures in European medical and scientific-philosophical thought of the time made opium their object of study, and allow us to reconstruct the transformation of medical theory and practice. The Early Modern period was a time of profound changes in the field of medicine, marked by the establishment of the first scientific societies and the arrival in Europe of large quantities of psy-

choactive substances from the New World, such as tobacco and chocolate, and from the East, such as coffee and tea. Moreover, it was during the Early Modern period, between the late seventeenth and early eighteenth centuries, that the recreational effects of opium were recognized for the first time, whereas it had previously been regarded solely as a narcotic and anodyne. Contemporary historiography has thoroughly examined how medicine has been used in the past as a tool to justify colonialism and how certain diseases were considered specific to particular regions or populations (Seth, 2018). However, less attention has been given to the ways in which drugs were used across different historical periods and ethno-geographic contexts, such as in the case of the different effect attributed to opium to the oriental people in the Early Modern period (Pierini, 2021). Western physicians knew the effect of the substances derived by the opium poppy since the ancient times, as we find its first certain mention in the Hippocratic treatises, and they were well acquainted with this plant which grew up spontaneously in Europe (Scarborough, 1995). The *Papaver Somniferum*, better known as opium poppy, is in fact rich in alkaloids such as morphine and codeine that, binding to the opioid receptors, produce effects such as analgesia, euphoria, respiratory depression and decreased gastrointestinal motility (Kapoor, 1995).

Following the medical knowledge of ancient authors such as Dioscorides and Galen, Early Modern physicians prescribed the drug as a remedy against a wide range of diseases including stomach disorders, vomiting, and cough. In Western civilization, from Antiquity to the Early Modern period, opium was not consumed for hedonistic or recreational purposes. Even if physicians administered opium only as a medicament, they were fully aware of its dangerous effect, as it reflected perfectly the Ancient Greek definition of *pharmakon*, a substance that, depending on the dosage, could act both as a curative or a poison. This classification however seemed not to work for oriental people as the Turks, Persians and Egyptians, who were supposed to be immune to the poisoning power of opium. The assumption we find in Francis Bacon's (1562-1626) *History of Life and Death* (1623) synthesizes a view shared by the most part of the Early Modern western physicians. They assumed that opium affected the oriental people in a completely different way compared to the Europeans.

The Turks find opium, even in large quantities, innocent and cordial, so that they even take it before a battle to give them courage. But to us, except in small quantities, and with strong correctives, it is fatal (Bacon, 1618).

The aphorism of Francis Bacon gives us a very meaningful description of the state of the matter. He is very clear and concise in describing the 'innocent and cordial' effect of opium on the Turks, who incredibly took it even

before the battle to become braver and scorn of danger. On the other side he referred to ‘us’, a category we can include the British and probably all the western people, who is very sensitive to the same drug and should use it only in a small dosage and with strong correctives. With respect to why opium acted so differently, however, Bacon offered no explanation. It was also commonly assumed that Eastern populations experienced pleasure from opium use, potentially leading to forms of addiction. In contrast, no evidence of systematic recreational consumption of opium appeared in Europe at that time. The question of why this debate emerged at that specific period and developed mostly in Britain remains significant. A key factor was the recognition of different cultures of intoxication adopted by extra-Europeans people. By the second half of the 16th century, medical treatises dealing with the use of foreign drugs, promptly translated and used by English physicians, had introduced new practices surrounding the use of intoxicants (Pierini, 2021).

Medical travel literature served as a crucial resource for examining alternative methods of drug consumption in the non-Western world during this period. Culturally specific practices, such as Turkish opium eating and Native American tobacco smoking, offered valuable points of comparison. These practices became significant benchmarks against which Western habits, particularly alcohol consumption, could be evaluated. Accounts of the consumption of opium, cannabis and hallucinogenic mushrooms by other cultures suggest that Europeans recognized in these practices the use of another well-known psychoactive substance not solely used for medical purposes: alcohol. In considering the ambivalent effects of opium on eastern peoples, this analogy proved particularly useful for European physicians examining the issue, as it allowed them to attribute these effects to cultural differences. Consequently, the belief emerged that opium could function as a “war drug” for Middle-eastern populations, inducing bravery and fierceness in battle, despite the well-documented effects of the substance being quite the opposite.

### 3. *How could opium became a war drug?*

The theme of oriental peoples consuming high doses of opium without negative consequences, and even experiencing increased bravery, appears frequently in many works from the sixteenth and seventeenth centuries. These works, however, generally refrain from providing a medical explanation for this phenomenon. Instead, the real explanation lies in the political significance of these works, mostly written by travelers and focusing on the Moors, who at the time were a source of fear in Europe. The Ottoman Empire, being both militarily threatening and geographically close, became the quintessential “other”,

serving as a point of comparison for reflecting the fears and expectations of the West (Formica, 2012, pp. 15–46). The western interest in the Ottoman Empire was relatively recent. While the fall of Constantinople in 1453 had revealed the existence of the Turks to the western world, it was only in the sixteenth century that they were seen as a new power to be reckoned with. In 1517, the Ottomans annexed Egypt and the Holy Land after defeating the Mamluks, and in the following decade, they attacked Hungary and achieved a decisive victory at the Battle of Mohács in 1526, later laying siege to Vienna in 1529. As western powers came into direct contact with the Turks, they began to explore this new enemy and assess its strength. Consequently, before 1530, there were very few works on the Ottoman Empire, except for some accounts of pilgrimages to Jerusalem. However, starting from this date, there was a proliferation of treatises about the Turks' lifestyle and political system.

The accounts of authors such as Pierre Belon (1518-1564) and Prospero Alpino (1553-1616), later translated into Latin by Carolus Clusius (1526-1609), as well as Nicolas De Nicolay (1517-1583), were disseminated throughout Europe and became essential for acquiring information to better understand and confront the Ottoman Empire (Clusius, 1589; Clusius 1605). In this context, the martial prowess of the Turks and their rapid conquests lent themselves to an explanation that involved the use of a nearly miraculous substance, opium, which was also used by Europeans. Thus, only the belief in opium's ambivalence could explain and justify the defeats of the Christians. The famous Hippocratic treatise *Airs, Waters, and Places* notes that Asians were generally weaker and more timid than Europeans due to the local climate's relative stability, lacking the significant temperature fluctuations found in Europe (Hippocrates, 400BC). Although there is no direct reference to this assumption in the works analyzed, from a theoretical perspective, the variability in the use and effect of opium would have compensated for this apparent lack of courage. In Europe, it was common to drink alcohol to face battles with more courage, and the connection between the use of hashish and ferocity in battle was also known, thanks to the popular account by Marco Polo (1254-1324) about the sect of the *Assassins*, ruthless warriors made nearly invincible through its use. The belief in the use of opium in warfare thus reflected the notion of considering opium as the intoxicating substance in eastern societies, just as alcohol was for Westerners, an analogy perfectly aligned with the cultural model of the time.

Even if at the beginning of the seventeenth century, there was a cultural milieu in Europe that was highly conducive to viewing opium as a "war drug", capable of producing different and specific effects on each population, over time the situation starts to change. Already in the first decade of the seventeenth century, English travelers visiting these outposts began reporting

on the use of opium. Among them, the preacher William Biddulph described how Turkish men would gather in coffeehouses, which he compared to the English pubs, to consume opium, and how this would cause them to lose touch with reality, engage in nonsensical conversations and experience visions (Biddulph, 1745). The poet George Sandys (1578–1644), reflecting on his journey from Venice to Constantinople in 1610, noted that the Turks were remarkably heavy users of opium, and that they carried it with them both in times of peace and war, believing it dispelled fear and instilled bravery. However, Sandys speculated that their behaviour was more likely due to their stubbornness. Although the belief that opium made the Turks courageous persisted for some time, it eventually became less prominent compared to efforts to understand why the Turks used it so differently, primarily for social rather than medical purposes, and whether this alternative use could also spread to Europe.

#### 4. *Comparative medicine and the domestication of foreign drugs*

Hippocratic and Galenic medicine of the time offered some possible explanations to the ambivalent effect of opium, but these did not fully convince the physicians and natural philosophers of the period, who sought new explanations.

During the sixteenth century, the increasing availability of printed works by Hippocrates and Galen provided the theoretical framework to justify the belief that opium had different effects on eastern peoples. The assumption that diseases arose based on a region's climate, geography, water, and diet was deeply rooted in European medical culture and, as a result, variations in the intensity of a disease or the effect of a drug were attributed to the specific anatomical and physiological temperament of the individual. Within the Hippocratic corpus, the text *Airs, Waters, and Places* particularly argues that physicians should consider the climate and geography of the places where patients live, as well as “the lifestyle of the inhabitants and their activities, such as whether they enjoy eating and drinking excessively, whether they are lazy, whether they love physical exercise and work, and whether they do not enjoy excessive eating and drinking” (Hippocrates, 400BC). This assumption was at the origin of the spread of racial stereotypes related to the different effects and abuse of opium, the primary intoxicant used by Muslim populations in the Middle East (Pierini, 2021). On the other hand, from a practical point of view it seems that physicians were more interested on the potential “domestication” of opium, understood as the consumption of larger quantities without risk, as the Orientals were believed to do (Breen, 2022).

The topic of opium domestication elicited differing opinions. In England, for instance, there were those like the physician Timothie Bright (1550/1–1615), who argued that the Turks' ability to use opium freely without harm, in contrast to its dangerous effects on the English, was evidence that it "was not made for us" (Bright, 1580):

That juice, or rather Milk of Poppy, which is brought out of Asia, named Opium, is not unknown to all the World, what a marvellous force it has in benumbing the sense of feeling, and utterly extinguishing the natural Heat of the Body, so that we fear to give thereof into the Body above the weight of two Grains, and those corrected with Saffron, Castoreum, and such like, let it cast the Patient into such a deep sleep, as he needed the Trump of an Arch-Angel to awake him. Now, the same Opium being taken of the Turks, Moors, and Persians, brings to their wearied and over travelled Bodies, a marvellous Recreation, in such sort, as they ordinarily use it therefore as a present Remedy, not in the quantity of two Grains or twenty, but even a whole Ounce or two at once.

Bright, who dedicated a treatise to the suitability of native English medicinal plants, believed that God created plants specifically for the people living in particular regions. He could not find any other explanation for why the same amount of opium, which he regarded as an Asian drug, would induce such a deep sleep in his fellow Englishmen that it would take the trumpet of an archangel to wake them, while for eastern peoples, it merely served as a delightful source of recreation. Bright was indeed convinced that the recreational and habitual use of opium by eastern peoples was unsuitable for the English.

A different view is expressed by Italian spagyric physician Angelo Sala (1576–1637), who published the *Opiologia* (1614), the first Western treatise entirely dedicated to the "nature, properties, true preparation and safe use of opium". In the frontispiece, Sala included an image of a Turk extracting opium from a poppy capsule to emphasize the Turks' familiarity with the substance. This was intended to suggest that Europeans could similarly "domesticate" opium, drawing a parallel to the recent example of tobacco. Tobacco, which was regarded as a potent substance like opiates, had been successfully introduced from the Americas and, within a few decades, became both a medicinal product and a recreational drug. The environmental and cultural context is therefore essential in determining a more liberal use of the substance, although it remains primarily confined to the medical lore. Sala's belief that "Christians" should become familiar with opium relied in the fact that he considered sleep and exemption from pain to be necessary things, both for healthy and sick men, as in the case of the other components of Galenic *non-naturalia* such as food and drink, "which sometimes are good and profitable to the bodie, and sometimes quite contrary, euen as nature disposeth of them for our good, or euill, howsoever in themselves they are

alwaies good, seeing without the no man can liue” (Sala, 1614). Sala is keen to point out that his desire is not to justify “abuses”, but rather for doctors to learn to treat better “simple people”, learning to administer opium at “the first incounter of the disease, when there is good hope of cure”, not forgetting the importance of “comfort and restore, to advance and bring them to their naturall rest, and to cease and qualifie their torments” (Sala, 1614).

From this series of considerations, we can deduce that, beyond the differing opinions of physicians, observing the ways in which eastern peoples consumed these substances led to a greater awareness of the effects of opium, and to its potential use as a recreational drug.

## 5. *The emergence of addiction*

During the latter part of the seventeenth century, there was a noticeable rise in the utilization of opium within the realm of European medicine. This period also marked the emergence of concerns regarding addiction, with medical practitioners and scholars noting instances of regular opium consumption and its resulting effects. In the chapter of his work on the Ottoman Empire that describes certain religious sects, the diplomat and member of the Royal Society, Paul Rycaut (1629–1700), introduced the notion of addiction with a completely new meaning, referring to the Turkish habit of consuming opiates instead of wine (Rycaut, 1668). Until then, the term “addiction” had appeared in the writings of some Protestant preachers, as well as a legal term derived from the Latin word “addicere”, meaning “to give favorable signs”, and had never been used in the context of substance dependency (Cree, 2018; Rosenthal and Faris, 2019).

The association with Turkish opium consumption indicates that observing different patterns among these peoples influenced the evolution of the concept we now define as drug addiction. At the same time, among Europeans, there was apparently no recognition of the pleasurable effects of opium or any potential for addiction until the early eighteenth century even if the phenomenon of frequent non-medical opium use was already well-known to travelers in the Middle East. Rycaut attributes this choice to unspecified traits of the eastern peoples’ personalities, such as a strong “inclination to yield to the course of their own nature”, or to the idea that opium “tends to enhance their natural lethargy” (Rycaut, 1668). In this way, opium consumption became both culturally and biologically justified, as the choice to use opiates was seen as a consequence of one’s inherent nature. Rycaut’s example also illustrates the tendency to attribute the differing effects of opium to an analogy

with the well-known state of drunkenness, suggesting that recreational opium effect was a result of a different cultural context use. From these examples, it is clear that Western physicians and intellectuals relied on comparisons with other cultures to develop their understanding of the effects of opium and, more broadly, of psychoactive substances. This process integrated concepts such as addiction and tolerance into European culture, while also perpetuating racial stereotypes.

Thomas Willis (1621–1675) was a physician and an influential member of the Royal Society of London, and his work represents a significant milestone in the development of new methods for investigating the effects of drugs in general and, in our case, narcotics. His pioneering studies in anatomy, particularly of the nervous system, and his mechanistic view of physiology led him to investigate the sites of action and the structures through which drugs exerted their effects. In doing so, he developed a complex theory that integrated clinical observation with anatomical investigation (Frank, 1990; Bynum, 1973). In his work *Pharmaceutice Rationalis* (1674), in addition to detailed anatomical, pathological, and clinical observations, he provides an accurate description of the drugs available at the time. In the important and extensive chapter on “opiates”, he explains how these substances are able to induce their psychoactive effects (Willis, 1678). In this context, it is unsurprising that attention was given to the Turks’ ability to consume large quantities without apparent serious side effects:

But that Opium is devoured in a great quantity by the Turks (I may add also some of our Countrymen having gotten by long Custom, as it were, a certain defence or Armour of proof against its poyson) unhurt, or at least without any danger of life; the Reason is because its Particles, although at first they are infestous and poysonous to the Spirits, yet by the frequent use they at length become more congruous and familiar; even as we have observed concerning the taking of Tobacco in a Pipe, which when ‘tis wont at first for a few days, to cause a Vertigo or dizziness, and oftentimes vomiting or purging, yea a cold Sweat with a trembling, and frequent faintings; yet afterwards we take it without any disturbance, yea at length with great delight (Willis, 1668).

From this statement, we can first infer that there was greater awareness of the phenomenon of tolerance and of set and setting. Willis clearly recognized the process that we now define as tolerance, possibly because it was no longer just about accounts of customs from distant lands, but about situations easily observed in everyday practice with both opium and tobacco. Also, Willis made it clear that there was not any racial difference in the Turks that would have justified any different effect, as he recognized how some of his countrymen developed some tolerance to its use. Even if he did not seem afraid of the growing consumption of these substances, by his statement we can deduce how opium consumption was a common habit at the time. His reference to

tobacco reinforces Angelo Sala's early-century prediction that opium could follow a similar path. Tobacco had initially been seen as highly dangerous due to its stupefying and hallucinatory effects. However, over time, it came to be viewed as a harmless product for social consumption, as its effects were described as pleasurable, making it more suitable for recreational use rather than medicinal purposes.

## 6. *The awareness of set & setting*

A turning point in the comprehension of this problem came only at the beginning of the eighteenth century, when the physician John Jones (1644-1709) published *The Mysteries of Opium Reveal'd* (1700), where he criticized the alleged danger related to the use of opium. He argued that all effects of the drug could be explained by the fact that it caused a 'pleasant Sensation', which led to a relaxation of all sensible parts of the body (Jones, 1700). A key point in the emergence of this revolutionary theory was that Jones believed his comprehensive understanding of the role of extra-drug variables, such as the user's environment, cultural context, and psychological state, had eluded other physicians. This recognition of the importance of 'set and setting' marked a significant shift in medical thought, highlighting how the subjective experience and surrounding circumstances can influence drug effects. Because of this psychosomatic explanation, he asserted that Western physicians should learn about the true effects of opium from eastern cultures, where the substance was used in non-medical contexts. This acknowledgment of the interplay between drug effects and cultural practices underscored a pivotal moment in history, where the understanding of psychoactive substances began to incorporate the broader social and environmental factors impacting their use:

I observed, That all our Modern Authors, and Physicians, receiving the Knowledge of Opium, its Effects, and Uses, from those Ancients, do use it only for the same Ends and Purposes as they did; and that our Modern Authors, living in these Western Parts of the World, very remote from the Eastern Countries, where it is used commonly, and in large Doses, by People in Health, to enliven, invigorate, and encourage them, and cause the brave, generous, and magnanimous Effects aforementioned (Courage, Euphory ecc). (Jones, 1700)

In this way, he recognized how central were the "Ends and Purposes" of the drug taking, which in this case seemed to be limited to giving pleasure and euphory to the consumer. This new approach to this aspect probably derived from the enthusiastic auto-experimentation Jones had undertaken several times, which probably led him to appreciate the stimulating and euphoric effect of opium. Jones highlighted that physicians traditionally ad-

ministered opium only to “sick people when they are going to bed”, which inherently limited their ability to observe its full range of effects. His most important point, however, is that by restricting opium use to purely medical contexts, doctors were missing the opportunity to understand how the drug could affect individuals who were not already compromised by illness. This practice denied any possibility of observing “those brisk effects” that might emerge in a healthier population or in different settings, where the psychological and social dimensions of drug use could be more fully appreciated. Jones recognized that this narrow medical application contributed to the belief that opium had different effects because its broader, more dynamic impacts were obscured by its association with treating illness. Thus, in his opinion, opium was just an empowered version of wine, with which it shared the same effect of causing “Swimming in the Head” (Jones, 1700). This realization underscored the importance of examining how opium functioned outside of a purely medical framework and suggested that its potential uses and effects were far more varied than previously understood. By acknowledging this limitation, Jones advocated for a more comprehensive approach to studying opium, one that considered the cultural and situational contexts in which it was used (Jones, 1700):

The moderate Dose in ordinary Use, to produce the following Effects, is from one to three Grains, (more or less) according to the Circumstance, Condition, Case, Constitution, Age, &c of the Person who takes it.

Jones precisely articulated the significance of non-pharmacological factors in determining the effects of opium, noting that the appropriate dosage varied from one to three grains based on various considerations such as the individual’s circumstances, condition, case, constitution, and age. With these assumptions we could claim how Jones recognized the importance of the *set & setting* and the role of intoxication as, even if he treated opium as a medical substance, he advocated its use on healthy people. He thought it was also a means to comfort and invigorate the sensitive soul, so that the psychotropic effect associated to the drug’s use gained a specific psychologic role (Kramer, 1979). However, the enthusiastic tone with which Jones spoke about opium, along with his claim of having an “intimate” understanding of the substance, suggests that he might have developed a form of dependence. Although the concept of alcohol addiction was recognized at the time, there seems to have been little awareness of the potential dangers associated with the continuous and excessive use of substances like opium. Despite the increasing use of opium during this period, the broader implications of dependency were not yet fully understood or acknowledged by society. Although Jones’s work was appreciated by most of the medical community of his time,

it did not exert the influence it perhaps deserved. This may have been due to his overly partisan emphasis on the merits of opium and, as a result, during the eighteenth century, his insights into the importance of *set and setting* in determining opium's effects were largely overlooked. Even in the eighteenth century, medicine remained heavily influenced by the theoretical frameworks of the universities where it was taught and Opium, while remaining a crucial component of various therapeutic systems, was still a subject of theoretical debate. In Friedrich Hoffmann's (1660-1742) system, it was considered a sedative, whereas John Brown (1735-1788) considered it a powerful stimulant. Numerous experimental trials were conducted on animals and humans as part of the controversy between proponents of its sedative effects and those who considered it a stimulant (Maehle, 1999). By the late eighteenth century, the most part of the medical community agreed that opium operates in two stages: first, as a stimulant, and then as a sedative (Maehle, 1998).

## 7. *Conclusions*

As we have observed, the history of opium in the Early Modern period illustrates that the progression of knowledge concerning psychoactive substances is not straightforward but, instead, it is influenced by numerous extra-scientific factors. Although the medical and pharmacological context of the time was still rooted in qualitative and humoral medicine, physicians demonstrated a remarkable capacity for observation that enabled them to recognize and understand complex phenomena such as tolerance and the significance of *set and setting*. This historical insight underscores how the interpretation and understanding of drug effects were shaped not only by scientific research but also by cultural, social, and environmental influences.

Also, the case study of opium in the Early Modern period shows how the transition from a medicinal remedy to a substance used for hedonistic purposes could be quite blurred. Furthermore, the varying effects of opium, shaped by individual mindset and social context, highlighted the significance of *set and setting* long before this concept was formally defined. Therefore, this historical example highlights the enduring relevance of understanding the broader conditions under which psychoactive substances are consumed, a principle that remains integral to contemporary psychedelic research. The case of opium in the Early Modern period shows how recognizing past discussions and debates about the variability in drug effects can provide valuable insights into the development of current policies to address the opioid crisis. It is interesting to note how until the eighteenth century there were no significant social problems associated with the use of opium, nor did lawmakers find it necessary

to regulate its consumption, reflecting a different awareness regarding its potential for abuse or addiction. The strict medical concern of ancient medical authorities progressively vanished in favour of a more liberal use of the drug but, although opium was eventually used for recreational purposes, its use remained under medical supervision. However, this did not prevent the spread of addiction, which was viewed as a moral issue rather than a medical problem, concerning the individual's personal conduct, and was generally tolerated by political authorities as long as it did not cause social order problems, unlike drunkenness. During the Early Modern period, opium did not appear to pose any threats to social stability, and consequently, no significant issues related to its consumption, or the behaviour of its users were documented.

From a therapeutical perspective, the evolution of opium use developed through the comparison across diverse cultural contexts and through varying notions of healing, this led to the belief that its application consistently served some form of medicinal purpose, even though it may have primarily aimed at inducing relaxation or facilitating sleep. Another significant insight from this case study is the recognition of how important the association between the consumption of certain psychoactive substances and ethnic identity is, which has historically led to the emergence of racial stereotypes and discrimination. In recent years, this was again quite evident in the case of crack addiction among African Americans (Murch, 2015; Meyers, 2004). In a similar vein, even though opium had been cultivated in Europe for centuries, it continued to be associated with the East well into the nineteenth century, demonstrating the enduring power of racial stereotypes established long ago.

Nowadays, it is widely understood that the opioid crisis is a multifaceted issue shaped by numerous contextual factors. Recognizing the significance of set and setting offers important insights for developing effective strategies to address the crisis. Addressing the opioid crisis requires a comprehensive approach grounded in a social-ecological framework that recognizes the complex interplay between individual behaviors and broader societal influences. Factors such as community conditions, interpersonal relationships, and societal norms significantly shape patterns of drug use and must be central to policy interventions. Legislators should prioritize harm reduction strategies, including the distribution of naloxone and access to clean syringes, which, despite criticism, have proven effective in reducing overdose deaths and improving public health outcomes (Mehboob, 2023).

Furthermore, policies must address the economic and structural drivers of the crisis, such as unemployment, deindustrialization, and socio-economic disparities that contribute to "deaths of despair" (Samuel *et al.*, 2020). Finally, stricter regulation and accountability for unethical pharmaceutical marketing practices are essential to curtail the systemic factors exacerbating opioid mis-

use. By integrating these dimensions into policymaking, legislators can adopt a comprehensive and informed approach to resolving the crisis.

In conclusion, the historical and comparative perspective can also illuminate how very old observations and experiences, even before the formal establishment of pharmacology and psychology, could help in shaping new approaches to studying and regulating psychoactive substances. For this reason, the model of *Set & Setting* should be applied to ‘rethink’ the whole history of drugs, allowing us to trace the spread and evolution of the medical and cultural elements surrounding the consumption of psychoactive substances.

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