**The Gordian knot of MDMA (Ecstasy).**

The gordian knot of MDMA (Ecstasy).

**DOI:**  10.32870/sincronia.axxv.n79.31a21

**Juan Enrique Fernández Romar \***

University of the Oriental Republic of Uruguay (URUGUAY)

**CE:** jfernandezromar@psico.edu.uy / **ORCID ID:**  0000-0001-5930-6512

**Leticia Aszkinas Browarski \*\***

University of the Oriental Republic of Uruguay (URUGUAY)

**CE:** jfernandezromar@psico.edu.uy / **ORCID ID:**  0000-0001-5930-6512

\* Degree in Psychology (Universidad de la República, Uruguay). Doctor of Health Sciences (National School of Public Health, Cuba); Master in Social Psychology (Universidad de la República, Uruguay); Specialized in Regional Processes of Evaluation and Accreditation of the Quality of Higher Education (Ibero-American Network for the Accreditation of the Quality of Higher Education – RIACES, Costa Rica). Professor of Social Psychology at the Faculty of Psychology of the University of the Oriental Republic of Uruguay.

(https://psico.edu.uy/directorio/referentes)

\*\* Degree in Psychology. Assistant Professor Grade II of the Institute of Clinical Psychology of the Faculty of Psychology (<https://psico.edu.uy/user/333>)

**This work is licensed under a** [*Creative Commons Attribution-NonCoercial 4.0 International License*](https://creativecommons.org/licenses/by-nc/4.0/deed.es)

**Received:** 24/03/2020

**Revision date:** 08/06/2020

**Accepted:** 05/11/2020

**SUMMARY**

This article reflects on the accumulation of meanings in drug use practices. The revision of the Greek concepts of *phármakon* and *pharmakós* as well as the notion of *fold* formulated by Gilles Deleuze serve as a basis for considering the current situation of MDMA, better known as Ecstasy, the synthetic drug of greater use in the world and that has revealed a great therapeutic potential.

In addition, the possible release of recreational and therapeutic use of MDMA is analyzed, based on the recent regulatory experience of cannabis tested inUruguay.

**Keywords**: Drugs. MDMA. Regulation of psychoactive substances.

**ABSTRACT**

In this article we reflect on the accumulation of meanings in drug use practices. The revision of the Greek concepts of phármakon and pharmakós as well as the notion of folding formulated by Gilles Deleuze serve as a basis to consider the current situation of MDMA, better known as Ecstasy, the synthetic drug of greater use in the world and that has revealed a great therapeutic potential. In addition, the possible release of the recreational and therapeutic use of MDMA is analyzed, based on the recent regulatory experience of cannabis tested in Uruguay.

**Keywords**: Drugs. MDMA. Regulation of psychoactive substances.

Psychoactive drugs function as a lens that enables the observation of new perspectives of relationship of the human being with himself and with his environment, placing himself on the threshold between the individual and the collective, between the radically singular and the cultural, as a paroxysm of the Deleuzian notion of fold. (Deleuze, 1994, p. 245)

Nature, culture and everything we understand to shape our subjectivity, as well as everything that is outside, in the world of objects and in social relations, should not be considered as ontologically distinct and separable entities but intertwined and folded with each other, defining multiple and dynamic forces and processes that produce recursive relationships. (Duff, 2016, p. 13).

Over time, the meaning given to the uses of psychoactive substances has been modified through sacramental practices such as festive or therapeutic. (Schultes, 2006, Furst, 1990). As the Spanish philosopher Antonio Escohotado has pointed out, in his General History of Drugs (1989), the vehicles of drunkenness became a multiple scientific enterprise, associated with the market and commerce, which ended up indignant to religion, provoking law, compromising the economy and tempting art.

Currently, drug use is both a personal issue and a public health and safety problem; and it is precisely at the intersection of these dimensions, between politics, economics and morals, that we managed to broaden the understanding of the matter.

In a certain way, what is defined as "the problem of drugs" functions as an analyzer (Lourau, 1977) that is, as a device capable of provoking the explicitation of the occult and that reveals the nature of what is instituted, highlighting the contradictions of a situation and enabling access to the elements that make up the structure of social political reality. (Fernandez, 2000, p. 13)

The complexity of the warp created around drugs generates a knot of meanings on the border between allowed and prohibited substances, since prohibitions do not always obey pharmacological criteria, but respond to conjunctural, historical and political reasons, derived from the criteria of analysis and regulation used. Simple examples of these contradictions are alcohol and tobacco, which despite having great addictive potential and causing multiple health damages are legal trade. (Fernandez, 2014)

Broadly speaking, psychoactive drugs are usually understood as those substances that in contact with the body produce a series of modifications in the central nervous system. (WHO, 2003)

The first drugs used by the higher hominids were the fruit of plants that deployed as a preservation mechanism certain secondary metabolites, that is, certain chemical defenses generated against potential dangers perceived in the environment that when consumed by some our ancestors modified their perception and behavior. (Akers, 2011; Wink, 2015; McKenna, 1999)

Human experiences marked by drug use acquired diverse readings and meanings. In hunter-gatherer cultures, the experiences of religious use of plants defined as sacred guided the ceremonies of communion with their gods, granting collective cultural identity and social cohesion to the community.

The Greeks of the classical era understood drugs as phármakon, remedy or poison depending on the knowledge of use, the occasion and the physical characteristics of the user. The effects of this or that substance are then guided by the interaction of these three dimensions and not specifically on the substance; without this implying denying the respective effects of each drug on the body. (Stumpf, 2006)

The pharmakos (changing only one letter) referred instead to the choice of a scapegoat; innocent sacrificial victim but capable of carrying all evils and whose death allowed to purge the evils that afflicted a human group. Pharmakos was both harm and solution. A formula as ambiguous as phármakon. (Fitzgerald, 2015; Harrison, 1991, p. 152)

The rituals and myths that made possible both the purification (katharsis) staged in the pharmakos varied substantially according to place and time (Cult of Bread; Dionysus or Bacchus among many others) and conjugated in different degrees: atonement for collective guilt; sacramental practices that reinforced the identity of that community; and were often followed by various forms of ecstasy and drunkenness.

With the passage of time instead of using a pharmakós (or scapegoat) for the absorption of the ominous and sick, the medicine will begin to use phármakon, as a suitable drug to treat the discomfort that was. It would no longer be necessary to make sacrifice to heal, but an astringent drug such as opium should be used in the face of a cholera epidemic.

Gradually, drugs, magic and medicine are differentiating. Drugs ceased to be circumscribed to the field of the sacred and the supernatural to begin to be seen as substances that generate predictable effects that can both heal and threaten the organism depending on their proportions because only the quantity distinguishes the remedy from the poison as paracelsus taught (1493-1541). (Gatenbein, 2017, p. 1)

The original stigma attached to psychoactive drugs derives from their intoxicating potential in a cultural framework that celebrates sobriety. At the end of the third century with the growing religious hegemony of Christianity in the ancient world all drunkenness began to be understood as the product of a human weakness.

The institutionalization of Christian creeds in different states and their conversion into an official religion, determined the prohibition of trance as a bridge between the ordinary and divine worlds, reaching its use even to be understood as a heresy.

In this way, the foundations were laid for a war against witchcraft, a legacy that ideologically fueled the war on drugs; as well as the risk of blurring the boundaries between investigation and conviction, between suspicion and guilt.

According to the proposals of Antonio Escohotado in his monumental *General History*   *of Drugs* (1989),for various reasons, the field of drugs began to produce stratifications, where some consumptions were "preferable" to others. For example, in Islam, the drunkenness produced by opium (where composure is maintained and precision activities can be carried out) was valued more than the consumption of alcohol that was considered stultifying and generating conflicts with work and family duties.

It is not easy to understand the prohibitionist will of drug substances that has prevailed in the world especially since the '70s of the last century since this requires a particular consideration of the numerous factors that converge in each case and in each substance in particular.

In any critical analysis of the entry of this or that drug to the list of prohibited substances, it can be observed that scientific, health, philosophical and religious reasons tend to amalgamate multiple economic interests and political projects of interest and pressure groups.

Likewise, the prohibition itself usually generates an increase in the added value of the substance that begins to be distributed in clandestine circuits without any type of quality control, which enhances its health risks. (Fernández, 2000, p.14).

At present some substances preserve and synthesize all the ambiguity and ambivalence that the Greeks deposited in the phármakon and pharmakós, being understood alternately as a remedy or poison, while their users are observed by government offices as innocent sacrificial victims, recruited in the pagan festivals of raves and secular ceremonies of acid-house. Although it is not a single ceremony or a single meaning that sustains the ritual.

MDMA pills bring together and condense all that primeval ambivalence becoming the contemporary epitome of recreational and festive drugs. They make up the great family of pastis (synthetic drugs in pills according to the psychedelic jargon of the Rio de la Plata) and the most popular social imaginary links them both to the atonement of "sins" and impurities through the psychotherapeutic ritual of detoxification of the habitual drug user who has been pointed out as a problematic user as well as with the youth that celebrates the modern jarana of Dionysus and the arrival of some spring, in the midst of an ecstasy officiated by satyrs and maeds dancing celebrating the renewal of life.

The substance 3,4-methylenedioxymethamphetamine better known by its semi-systematic name abbreviated MDMA occupies a privileged position among the designer drugs being one of the most consumed. It is a synthetic base that derives from phenylethylamine and for structural reasons is linked to both amphetamines and mescaline, a powerful psychoactive.

It was first synthesized in the laboratories of the pharmaceutical company Merck in 1912 although its potential uses remained unnoticed until the early '40s being tested by the CIA (Central Intelligence Agency) as "truth serum". (Davenport-Hines, 2004, p. 463).

After a series of trials it fell back into oblivion until Alexander "Sacha" Shulgin (1925-2014), a famous American psychopharmacologist of Russian descent rediscovered it and began to experiment personally with this substance in the decade of the '60s.

As it is a drug that increases the release of certain neurotransmitters in the nerve terminals producing sensations of intense satisfaction, this led Shulgin to propose it as a good adjunct to couple psychotherapies, in treatments of depression and post-traumatic stress.

In general terms, MDMA is a white crystalline substance that is usually consumed orally. Its consumption increases the release of serotonin, dopamine and norepinephrine while inhibiting the reuptake of those neurotransmitters and the degrading action of monoamine oxidase. All this leads to an accumulation of serotonin, dopamine and norepinephrine in the intra- and extracranial synaptic spaces similar to those induced by amphetamine and cocaine. (Gainza et al, 2003, p.114; Tancer & Johanson, 2007).

It is considered an empathogenic drug, that is, it generates empathy (Muñoz, 2017) that also produces euphoria and hyperactivity, decreases anxiety, increases muscle tension, dilates the pupils and reduces the sensation of physical pain.

The most frequent acute effects due to repeated or abusive consumption are anxiety, anorexia, sweating, palpitations, bruxism, nausea and mental confusion.

It can present residual effects after consumption such as tiredness, irritability and mood disturbances. Its prolonged use is associated with adverse phenomena such as neurotoxicity and cognitive impairment.

The first pseudonym of the MDMA was Adam, for the eventual catharsis that induced promoting the rebirth of an "inner child" illuminated in psychotherapy sessions. In a therapeutic device or in the arms of someone dear who has consumed this substance feels more confident and seeks greater intimacy while when this happens in a large dance hall the experience is transformed into a subtle and polymorphous encounter.

Between 1978 and 1984 MDMA became a recurring topic of research and a great promise for the future of brief psychotherapies. In addition to Shulgin other researchers such as psychiatrist and anthropologist Stanislav Grof, founder of transpersonal psychology and pioneer of psychological research of altered states of consciousness; his colleague, the Chilean psychologist Claudio; as well as the Californian psychotherapist Leo Zeff and the renowned pharmacologist David Nichols, famous for his research in neurotransmitters; all of them defended the therapeutic potential of MDMA. (Passie, 2018)

It should be clarified that in the historical review of this substance there is usually a certain degree of confusion with the evolution of other very similar phenylethylames, in particular with MDA (3,4-methylenedioxianphetamine) and 3,3,4 methyldioxyethylanphetamine (MDEA) that revealed early a greater toxicity and were outlawed in the '70s although they still continue to appear as frequent adulterants of MDMA. (Passie, 2018; Davenport-Hines, 2004, p. 464)

The initial enthusiasm with all these substances was great and both Shulgin and the other researchers of the first hour sought to maintain their use in the restricted frameworks of psychotherapeutic clinics in search of a more widespread scientific legitimacy.

However, the technical ease of its synthesis and its euphoric effects made it a fashionable drug in the North American and European nightclubs of the '80s in which there were numerous situations of abuse and lack of quality controls.

In 1985 the US agency DEA (Drug Enforcement Administration) included MDMA in Schedule I of very dangerous substances triggering the planetary prohibition of production and sale of it.

Far from stopping the expansion of its use, the prohibition generated an increase in its price, a deterioration of its average quality and the development of a counterculture that adopted it as an ideological password for recreation and search for proxemic blurring typical of raves party.

The latest global reports of the United Nations Office on Drugs and Crime (UNODC, 2018) observe a constant growth of new psychoactive substances, mainly of synthetic origin, noting that Ecstasy together with other amphetamine-type stimulants, are the second most consumed type of drugs worldwide, involving 21 million people. Likewise, according to the report of the CICAD – Inter-American Drug Abuse Control Commission – for the Americas– (CICAD, 2019) MDMA is the most consumed drug in Latin American countries of amphetamine-type stimulant substances.

In the VI National Household Survey on drug consumption conducted by the Uruguayan Drug Observatory (OUD, 2016) it was observed that 2% of the population had tried a synthetic drug at some time in their lives. Although the prevalence is relatively low, its steady growth should be noted. While in 2001 the consumption of this type of substance was expressed in 0.1 of the population interviewed in 2014, it stood at 1.4%.

In another study that analyzed the drug use of the university population (OUD, 2015) the prevalence of MDMA use was 2.8%.

These data are consistent with studies that refer to the socioeconomic profile of people who use MDMA, as well as with the increase in the use of this drug in people of higher age range, since they usually begin to consume around 21 years, without observing significant differences by sex (Camarotti, 2010; p.145; OUD, 2015).

In 2015, the Faculty of Humanities and Education Sciences and the National Secretariat of Drugs of Uruguay conducted an exploratory study on the use of synthetic drugs in Montevideo (Suárez & Rossal, 2015) raising as guiding questions the forms of access to substances, experiences and perceptions of users of synthetic drugs, knowledge about the risks and effects that users handle, in what contexts they use them and what meanings they attribute to them.

In the preliminary report of this work it is observed that users rather than looking for the stimulating effects of the substance, feel seduced by the empathogenic effects of the substance, where the altered state of consciousness, the absence of sadness and aggressiveness and the possibility of experimentation with music are highlighted. This study, from its results, recognizes the chemical manipulation of mood as an extremely significant dimension.

In Uruguay, MDMA users are mostly young people living in Montevideo, from medium and high socioeconomic segments, with a modality of approach to drugs defined by polyconsuming.

Although the scientific interest in MDMA as a potential therapeutic resource was maintained since Shulgin's first experiences in the last fifteen years, there has been a noticeable increase in research aimed at staging an effective and efficient way of psychotherapy based on the use of this substance. (Chabrol, 2013; Hutchison & Bressi, 2018; Thal & Lommen, 2018; Bender, 2005)

Uruguay does not escape this trend, with MDMA being a frequent topic in regional academic communications and exchanges despite the fact that funding has not yet been obtained for lines of research that are not ethnographic or epidemiological.

MDMA is an empathogenic substance that generates experiences of great intensity with pleasurable effects that make people friendly and open for a few hours.

It disinhibits communication, decreases fear and suspicion, fosters sympathetic encounters, increases acceptance of oneself and others, and intensifies self-confidence. Hence its potential use in therapy.

It does not generate loss of consciousness, but increases the possibilities of perception of linking subtleties and artistic details.

It induces dancing and friendly contact with others. Unlike other stimulants such as cocaine, it does not encourage the exercise of violence. In the electronic parties of mass use of MDMA, the fights, grievances and the different forms of possible manifestation of gender-based violence are minimized.

It is not an addictive drug and does not produce typical withdrawal syndrome or psychological dependence, although it does develop tolerance.

It is not a substance of daily use and its frequent use dilutes the charm of its effects making it less effective. For that reason it cannot be considered as a drug of happiness in the style of the "soma" consumed by the characters of the novel Brave NewWorld (1931) by the British philosopher Aldous Huxley.

It is a paradoxical synthetic substance since it does not induce introversion in the world of electronic stimuli but face-to-face connectivity.

Most of the reported morbidity and mortality is associated with the adulteration of the substance, polyconsumum and not so much with the drug itself.

As in much of the world, electronic parties have multiplied in the last decade in Uruguay and with it the consumption of pills and press information.

An experience of sample control at a party showed that a third was adulterated, which indicates the risk that its illegality entails. (Garat, 2018)

In any case, such quality tests generated controversy since they can be understood as a preventive action but also as an act of condescension with a prohibited substance and contemplation of its consumption.

In Uruguay, it has been more than five years since the institutionalization of the new regulatory framework for cannabis; the famous Law No. 19,172 enacted in 2013: Marijuana and its derivatives. State Control and Regulation of production, acquisition, storage, marketing and distribution and most of the implementation difficulties (delays in the allocation of licenses for cannabis producers; repeated postponements for the start of sale in pharmacies; etc.) appear in 2019 overcome or in the process of being overcome.

Although the impact of Uruguay's legislative drift in relation to cannabis has been overshadowed by more forceful measures such as that adopted by Canada or nine other States of the United States that admitted its recreational use anyway by virtue of its demographic dimensions (three and a half million inhabitants), this small country continues to constitute an interesting social and political laboratory in relation to the ongoing processes of drug standardization.

By normalizing we mean what Oriol Romaní (2017, p.72) has defined as"[...] a set of processes that have led to the sociocultural recognition of the plurality of drug uses, and the meanings associated with them."

And more particularly to what their compatriots Pere Martínez Oró and Xabier Arana (2015) have redefined as sociocultural normalization, understanding as such the result of the cultural settlement of multiple substances, a process in which drugs have ceased to circulate on the margins of society to be accepted as compatible at certain times and specific contexts.

In this sense, if a positive valuation consensus of the regulatory experience of cannabis is finally established, perhaps it is time to start discussing a new regulation for other substances – such as MDMA – that have qualitative advantages that outweigh the harms of their prohibition andpersecution.

**References**

Akers, B.; Ruiz, J.; Piper, A. & Ruck, Carl. (2011). A Prehistoric Mural in Spain Depicting Neurotropic Psilocybe Mushrooms. *Economic Botany, 65*(2), 121-128. OJI:10.1007/s12231-011-9152-5

Bender, E. (2005). FDA Approves Study of Ecstasy In Some Terminally Ill Patients. *Psychiatric News,40*(2), 46-46. DOI:10.1176/pn.40.2.00400046a

Camarotti, C. (2010) Practices, discourses and new spaces of sociability around the consumption of Ecstasy by young people from middle sectors of the City of Buenos Aires. Thesis to opt for the title of Doctor in Social Sciences, Faculty of Social Sciences, University of Buenos Aires. <http://cdsa.aacademica.org/000-106/544.pdf>

Chabrol, H. (2013) MDMA Assisted Psychotherapy Found to Have a Large Effect for Chronic Post-Traumatic Stress Disorder. *Journal of Psychopharmacology,*vol. 27, no. 9, 2013, pp. 865–866., DOI:10.1177/0269881113495119.

Inter-American Drug Abuse Control Commission CICAD (2019). Report on Drug Use in the Americas. <http://cicad.oas.org/Main/ssMain/HTML%20REPORT%20DRUG%202019/mobile/index.html>

Deleuze, G. (1994). Difference and repetition. London: The Athlone Press.

Duff, C. (2016). *Assemblages of health: Deleuzes empiricism and the ethology of life*. Australia: Springer. DOI:10.1007 / 978-94-017-8893-9

Escohotado, A. (1989). General history of drugs. Madrid: Alianza.

Fernandez, J. (2000). Cursed drugs. The hologram of drugs and other tests. Montevideo: Nordan.

Fitzgerald, J. (2015). *Framing drug use: Bodies, space, economy and crime*. Basingstoke: Palgrave Macmillan.

Furst, P. (1990). *Flesh of the gods: The ritual use of hallucinogens*. Prospect Heights, IL: Waveland Press.

Gainza, I.; Nogué, S.; Martinez, C.; Hoffman, R. S.; Burillo-Putze, G.; Dueñas, A.; Gómez, J. & Pinillos, M. A. (2003). *Drug poisoning. Annals of the Health System of*Navarre. <https://recyt.fecyt.es//index.php/ASSN/article/view/5014/4252>

Garat, G. (24 Mar. 2018) "MDMA: The Pill Of Discord." *La Diario*. https://findesemana.ladiaria.com.uy/articulo/2018/3/mdma-la-pastilla-de-ladiscordia/.

Gatenbein, U. (2017). Poison and its dose: Paracelsus on Toxicology. In Wexler, Plhilipp. *Toxicology in the Middle Ages and Renaissance. London*: Elsevier, 1-10. <https://www.elsevier.com/books/toxicology-in-the-middle-ages-and-renaissance/wexler/978-0-12-809554-6>

Harrison, J. (1991). *Prolegomena to the Study of Greek Religion*. Princeton: Princeton University Press. ISBN 0-691-01514-7.

Hutchison, C. & Bressi, S. (2018). MDMA-Assisted Psychotherapy for Posttraumatic Stress Disorder: Implications for Social Work Practice and Research. *Clinical Social Work Journal*. DOI:10.1007/s10615-018-0676-3

Lourau, R. & Lapassade, G. (1977) Institutional analysis. In: Claves de la sociología (pp. 56-74). Barcelona, Spain: Laia.

Martinez, P. & Arana, X. (2015). What is standardisation in the field of drug use?  *Revista Española De Drogodependencias,*3, 27-42. <https://www.aesed.com/descargas/revistas/v40n3_2.pdf>.

McKenna, T. (1999). Food of the gods: The search for the original tree of knowledge: A radical history of plants, drugs and human evolution. London Rider.

Muñoz, D. (2017) Patterns of synthetic drug use. Pharmacology of 2C-B. <https://ddd.uab.cat/record/175860>.

Uruguayan Observatory of Drugs OUD (2015). *First pilot study on drug use in university students in Uruguay.* [https://www.gub.uy/junta-nacional-drogas/comunicacion/publicaciones/primer-estudio-piloto-sobre-consumo-de-drogas-en-estudiantes#](https://www.gub.uy/junta-nacional-drogas/comunicacion/publicaciones/primer-estudio-piloto-sobre-consumo-de-drogas-en-estudiantes)

Uruguayan Drug Observatory OUD (2016). *VI National Household Survey on Drug Use,* *2016.* Research report. Uruguay: National Drug Board. <https://www.gub.uy/junta-nacional-drogas/comunicacion/publicaciones/vi-encuesta-nacional-en-hogares-sobre-consumo-de-drogas-2016>

Passie, T. (2018). The early use of MDMA ('Ecstasy') in psychotherapy (1977–1985). *Drug Science, Policy and Law, 4,*205032451876744. DOI:10.1177/2050324518767442

Roma, O. (2017). Youth,participation, health and drugs. *Metamorphosis,*64-79. [http://revistametamorfosis.es/index.php/metamorfosis/article/view/55](http://revistametamorfosis.es/index.php/metamorfosis/article/view/55#_blank)

Schultes, R.; Hofmann, A. & Rätsch, C. (2006). *Plants of the gods: Their sacred, healing and hallucinogenic powers*. Rochester, VT: Healing Arts Press.

Stumpf, W. (2006). The dose makes the medicine. Drug Discovery Today, 11(11-12), 550-555. DOI: 10.1016/j.drudis.2006.04.012

Suárez, H.,and Rossal, M. (compilers) (2015). *Synthetic trips. Studies on the use of synthetic drugs in contemporary Uruguay.* Uruguay: Universidad de la República/Junta Nacional de Drogas.

Tancer, M., & Johanson, C. (2007) The effects of fluoxetine on the subjective and psysiological effects of 3,4-mathylenedioximethamphetamine (MDMA) in humans. Psychopharmacology, 189(4th, 565-573. <http://doi.Org/10.1007/s00213-006-0576-z>

Thal, S. & Lommen, M. (2018) Correction to: Current Perspective on MDMA-Assisted Psychotherapy for Posttraumatic Stress Disorder. *Journal of Contemporary Psychotherapy,*vol. 48, no. 2, 2018, pp. 109–109., DOI:10.1007/s10879-018-9382-2

United Nations Office on Drugs and Crime UNODC (2018). World drug report. <https://www.unodc.org/wdr2018/>

World Health Organization WHO (2003)*. Expert Committee on Drug Dependence thirty-third report*. OJI:0512-3054

Wink, M. (2015). Modes of Action of Herbal Medicines and Plant Secondary Metabolites. *Medicines, 2*(3), 251-286. DOI:10.3390/medicines2030251