Review of the experiences of users of methaqualone and methaqualone derivatives. An analysis of online forums

Przegląd doświadczeń użytkowników metakwalonu i pochodnych metakwalonu. Analiza forów internetowych

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Abstract
The aim of this review article was to collect and analyze the available information on methaqualone and its derivatives reported by users in dedicated online forums. Methaqualone is a sedative-hypnotic drug that has been widely used for medical purposes in the past, but is now illegal in most countries due to its high abuse potential. The review collected information on doses, routes of administration, desirable and side effects of intoxication and other relevant aspects of the abuse of these compounds. The results of the study suggest that methaqualone and its derivatives continue to be used by some individuals despite their illicit status and potential health risks. The review, in the absence of other more reliable toxicological data, provides valuable insights from direct users on the use of these substances.

Keywords
Methaqualone, Sedative-hypnotic drug, Online forums

Streszczenie
Celem tego artykułu przeglądowego było zebranie i analiza dostępnych informacji na temat metakwalonu i jego pochodnych zgłaszanych przez użytkowników na dedykowanych forach internetowych. Metakwalon jest substancją o działaniu sedatywno-hipnotycznym, który w przeszłości był szeroko stosowany w celach medycznych, ale obecnie jest nielegalny w większości krajów ze względu na wysoki potencjał nadużywania. W przeglądzie zebrano informacje na temat dawek, dróg podania, pożądanych i ubocznych skutków odurzenia oraz innych istotnych aspektów nadużywania tych związków. Wyniki przeglądu sugerują, że metakwalon i jego pochodne są nadal używane przez niektóre osoby pomimo ich nielegalnego statusu i potencjalnego ryzyka dla zdrowia. **Przegląd, przy braku innych bardziej wiarygodnych danych toksykologicznych, dostarcza cennych spostrzeżeń od bezpośrednich użytkowników na temat używania tych substancji**.

Słowa kluczowe
Metakwalon, Sedatywno-hipnotyczny lek, Fora internetowe

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Introduction

Over the past two decades, a growing concern has emerged worldwide over the illicit designer drug market. Novel psychoactive substances (NPS) have been increasingly used as substitutes for conventional drugs to mimic their effects while avoiding legal restrictions [1,2]. The internet, including online forums dedicated to NPS users, has facilitated the development of the NPS market by providing knowledge on the existence of substances, their properties, routes of administration, dosages, and sources of acquisition. These forums are valuable for legislators, early warning systems, and forensic toxicologists as they provide information on the appearance of new substances on the market, their prevalence, and the subjective symptoms of poisoning, doses used, and routes of administration [3,4].

Methaqualone (2-methyl-3-(2-methylphenyl)-4-quinazolinone), also known as Quaaludes, is a sedative-hypnotic drug that was initially introduced in the 1960s as a sleeping aid, advertised as a safer alternative to barbiturates [5]. However, it was found to be addictive and widely abused for recreational purposes, leading to numerous cases of overdoses, especially when taken with alcohol, and the facilitation of sexual assaults. These events resulted in legislative restrictions and the eventual withdrawal of methaqualone from use (for a comprehensive review describing the history of methaqualone use and pharmacological properties, see [5]). While methaqualone abuse has significantly reduced in most countries worldwide, there are still regions where it remains problematic [5,6]. In the 1960s, besides methaqualone, several of its analogues were synthesized and subsequently tested for medicinal use, but the vast majority of them were never marketed due to adverse effects (Figure 1.) [5]. In recent years, previously unreported identifications of methaqualone analogues in illegal products and isolated cases of poisoning have been reported globally [7–14]. Most of these compounds have limited understanding and limited literature data on their properties. Thus, this study aimed to collect the reported experiences of methaqualone and its analogues described by users in online forums, including the doses used, routes of administration, desired and side effects of intoxication, and other relevant information related to their use (Table I).

Characteristics of online sources

The studied websites vary in nature or purpose and therefore include a range of different types of information. Some of them are international forums dedicated to or having specific dedicated threads to drug users who share general information, their experiences and insights (Reddit.com; Drugs-forum.com; Bluelight.org). Such forums often self-describe that their mission is harm reduction, hence the content includes such details as recommendations for dosages, routes of administration, the safety precautions of taking particular drugs and possible side effects. Besides these forums, there are also websites that are databases created by organizations or a dedicated community with the aim of organizing knowledge about psychoactive substances in an encyclopedic way (Psychonautwiki.org; Erowid.org; Isomerdesign.com). For well-known and well-studied substances, these sites base the information provided on the scientific literature, while for less well-studied substances, the information comes largely directly from users and their experiences. Another relatively useful source of data are the websites of organizations that conduct anonymous laboratory testing of user-submitted samples of drugs (DrugsData.org; Wedinos.org). Data published there include the appearance and origin of the sample and the results of analyses, sometimes including GC-MS spectra or other analytical data.

All these pages were carefully searched for relevant threads using the names and synonyms of methaqualone and its analogues as keywords. Particular attention was given to those threads that were the most popular, most commented on and to the information that was frequently recurring. Isolated, non-credible reports of intoxication symptoms, effective doses, or duration of action were not taken into account in the preparation of Table I and the subsections on individual compounds. It should be noted that reliable and comprehensive data obtained through scientific research is only available for methaqualone, and the information we have collected on methaqualone analogues is mostly an aggregation of the knowledge provided by users of these substances. As such available information is not subjected to any form of verification, special care and a critical approach should be taken when using these data.

Methaqualone

Methaqualone is a well-recognized drug with a history of over half a century of use and its pharmacological properties and side effects are well-established [5,15,16]. The drug is typically administered orally in tablet or capsule form, with a typical dose range of 150-300 mg. However, chronic use can lead to tolerance and altered effective dose sizes (Table II). Small doses have a sedative, anxiolytic, and relaxing effect, while larger doses cause euphoria, dizziness, nausea, increased libido, muscle relaxation, short-term memory loss, and, in severe intoxication cases, loss of motor control, unconsciousness, and respiratory depression [5,17]. Other routes of ingestion include smoking (with cannabis mixtures - a particularly popular variant in South Africa), insufflation, sublingual, and injections, but they are less common.

Online forums are a rich source of information related to the use of methaqualone, with the oldest mentions dating back to the first years of the 2000s [18,19]. Recently, there have been further mentions reporting the use of the drug [20–22]. Many users recall the popularity of methaqualone in the 1970s and 1980s, particularly in the USA, and describe their use of the drug positively, generating interest of other users (Table II). The drug's depiction in popular culture, such as in Martin

***Table I.** Summary of the routes of administration and doses, duration, desired and side effects induced described in online forums*
***Tabela I.** Zestawienie dróg podania i dawek, czasu trwania, pożądanych i wywołanych skutków ubocznych opisywanych na forach internetowych*

Name (other names)	Routes of administration, typical doses used [mg].	Duration of effects	Desired effects	Side effects
Methaqualone (Quaalude, Mandrax)	**Oral** Low 50-150 Medium 150-300 High >300 **Smoking/Vaporizing** **Intranasal** **Sublingual**	**Oral** 5-8 h Peak intensity after 1-2 h	Sedation, Euphoria, Relaxation, Increased libido, Anxiolytic, Muscle relaxation	Dizziness, Impaired motor control, Loss of consciousness, Impaired short-term memory, Respiratory depression, Impaired vision, Constipation
SL-164 (Dicloqualone)	**Oral** Low 50-150 Medium 150-300 High >300 **Smoking/Vaporizing** **Intranasal**	**Oral** 3-6 h Peak intensity after 45 min	Euphoria, Relaxation, Anxiolytic Hallucinations, Delusion, Muscle relaxation	Severe tremors, Seizures, Loss of consciousness, Impaired short-term memory, Impaired speech Hematuria, Methemoglobinemia
Nitromethaqualone (NMQ)	**Oral** Low <10 Medium 10-25 High >25 **Intranasal** Low <30 Medium 30-40 High >40 **Smoking/vaporizing** Medium 5	**Intranasal** 1-3 h Peak intensity after 1 h	Euphoria Sedation, Relaxation, Increased libido, Anxiolytic	Physical discoordination, Muscle twitches, Itching, Dizziness, Loss of consciousness, Impaired speech
Mebroqualone (MBQ)	**Smoking/Vaporizing** Low 8-50 Medium 50-100 High >100 **Sublingual** Low 15-20 Medium 20-50 High >50 **Oral** Medium 100 **Intranasal** **Rectal**	**Smoking/vaporizing** 0.5-2 h Peak intensity after 5-10 min **Sublingual** 3-4 h Peak intensity after 20-60 min	Euphoria (short-lived and strong), Sedation, Relaxation, Anxiolytic	Severe physical discoordination, Impaired vision, Tremors, Nystagmus, Akathisia, Impaired short-term memory, Numbness
Ephinazone	**Oral** Low <100 Medium 100-200 High >200 **Smoking/vaporizing** Medium 20-80 **Rectal**	**Oral** 3-4 h Peak intensity after 1 h **Smoking/vaporizing** 0.5-1 h Peak intensity after 5-10 min	Euphoria, Sedative, Anxiolytic, Sociability	Dissociation, Jaw tension, Impaired hearing
Methylmethaqualone (MMQ)	**Oral** Low 50-100 Medium 100-200 High >200 **Smoking/vaporizing** Typical 5-25 Other reports indicate 1-4mg as "potent" **Sublingual** **Rectal**	**Oral** 3-6 h **Smoking/vaporizing** 0.5-1 h Peak intensity after 5-10 min	Sedation Euphoria Relaxation	Severe physical discoordination, Impaired vision, Seizures, Tremors, Impaired short-term memory
Etaqualone (ETQ)	**Oral** Low 200-300 Medium 300-400 High >400 high	**Oral** 1.5-5 h Peak intensity after 30-60 min		

Name (other names)	Routes of administration, typical doses used [mg].	Duration of effects	Desired effects	Side effects
Etaqualone (ETQ)	**Smoking/vaporizing** Low <30 Medium 30-80 High >80 **Sublingual** Low <100 Medium 100-200 High >200 **Intranasal** **Rectal**	**Smoking/vaporizing** 0.5-1 h Peak intensity after 10 min	Sedation, Relaxation, Euphoria	Physical discoordination, Impaired vision, Impaired short-term memory Impaired hearing, Numbness

The data given are derived from a thorough authors' review of user descriptions in the online forums. The routes of administration, and the desired and side effects induced, are listed in the order of frequency reported by users. The ranges of typically used doses listed are based on the intensity of symptoms described by users. The low range corresponds to doses causing noticeable but low-intensity effects. The medium range corresponds to doses considered by users to be effective doses producing the desired effects of intoxication. High doses are indicated as predominantly causing adverse effects. It should be noted that the effects listed do not necessarily correspond to the frequency of symptoms actually occurring and may not include all of them. The symptoms listed only reflect the most commonly reported effects by users. It is also important to understand that the doses described, along with the duration of action, may be different in reality and vary from person to person due to personal differences and due to the unknown and possibly varying composition of specific samples.

Podane dane pochodzą z dokładnego, dokonanego przez autorów przeglądu opisów użytkowników na forach internetowych. Drogi podania oraz wywoływane działania pożądane i uboczne są wymienione w kolejności częstości zgłaszania przez użytkowników. Wymienione zakresy typowo stosowanych dawek oparte są na intensywności objawów opisywanych przez użytkowników. Niski zakres odpowiada dawkom powodującym zauważalne, ale mało intensywne skutki. Średni zakres odpowiada dawkom uznawanym przez użytkowników za dawki skuteczne, wywołujące pożądane skutki odurzenia. Dawki wysokie są wskazywane jako dawki w przeważającej mierze powodujące działania niepożądane. Należy zauważyć, że wymienione skutki nie muszą odpowiadać częstotliwości faktycznie występujących objawów i mogą nie obejmować ich wszystkich. Wymienione objawy odzwierciedlają jedynie najczęściej zgłaszane przez użytkowników efekty. Ważne jest również, aby zrozumieć, że opisane dawki, podobnie jak czas działania, mogą być inne w rzeczywistości i różnić się u poszczególnych osób ze względu na różnice osobnicze oraz ze względu na nieznany i ewentualnie zmienny skład konkretnych próbek.

Scorsese's film The Wolf of Wall Street and actor Bill Cosby's use of Quaaludes as a date rape drug, has also generated interest. Another popular thread topic is finding original old pharmaceutical preparations of methaqualone, which is met with enthusiasm, and the desire to try the drug is frequently expressed by users [23]. However, most indicate the drug's lack of availability and discuss possible sources of obtaining it, such as from South Africa.

Homemade synthesis of methaqualone is also frequently discussed, with users sharing detailed instructions on various synthesis methods and optimization techniques [20]. This is a particularly hazardous trend, as one of the most commonly used precursors in the synthesis of methaqualone is o-toluidine, a highly carcinogenic compound [5]. Most of the users seem to be aware of this danger and a frequent issue discussed is the attempt to reduce the harm of the homemade final product. In addition to attempts to synthesize methaqualone, the demand for the drug has led to an increase in the prevalence of its analogues, which pose a significant risk to users [5,8–12]. Some may unintentionally use methaqualone analogues when the preparation they take instead of methaqualone proves to be a derivative of this drug. Alternatively, some users may deliberately take methaqualone analogues to induce similar effects. In either case, the analogues may cause unpredictable effects, and doses that result in overdose may be much lower than for methaqualone alone, leading to dangerous intoxication.

SL-164

SL-164 (5-chloro-3-(4-chloro-2-methylphenyl)-2-methyl-4-quinazolinone), also known as dicloqualone, is a dichlorinated derivative of methaqualone that was synthesized in Japan in the late 1960s but was never introduced for medical use [24]. The first references in online forums to this analogue identified by the authors date back to May 2019 [25,26]. Initially, the substance generated a lot of interest and enthusiasm among users, as when taken orally it produced euphoria, relaxation and effects described as similar to GHB and carisoprodol. The most commonly reported effective route of administration was oral, with a duration of several hours and a peak intensity of symptoms after approximately 45 minutes. However, other routes of administration such as smoking and nasal ingestion were also mentioned, but the effects were described as much weaker or not noticeable (Table I).

Currently, threads related to the use of SL-164 mainly contain warnings about the substance due to its ability to cause strong convulsions and seizures even at the smallest doses required to achieve the desired effect (approximately 200 mg orally). Users often describe problems with body control and movement, and in cases of severe poisoning, complete paralysis and inability to move the body are observed. Loss of consciousness is also common, along with a loss of short-term memory (Table II). Cases of simultaneous use of alcohol to enhance the effects of this analogue are also reported.

One alarming issue regarding the use of SL-164 is the purity of the substance being consumed. Users have reported that the product may contain residues of the precursor used in its synthesis, 4-chloro-o-toluidine, which has been shown to have strong carcinogenic properties and can cause bladder damage and hematuria in cases of acute poisoning [27]. Indeed, this precursor has been detected in SL-164 samples seized in Europe in 2021 and 2022 by drug testing organizations sent by their users [28,29].

Currently, two cases of SL-164 poisoning have been reported in the literature [7,13]. In the first case, a 22-year-old man who

Table II. *Collection of experiences of taking methaqualone derivatives described in online forums (original spelling)*
Tabela II. *Zbiór doświadczeń związanych z przyjmowaniem pochodnych metakwalonu opisanych na forach internetowych (pisownia oryginalna)*

Experiences described on online forums by users	Quote
Experiences of methaqualone use during the years of its peak popularity	I am 62, in my late teens are until about age 22. You could get real pharmaceuticalmetaqualone. It was the main party drug for us in central USA. You could even occasionally find doctors who would prescribe you bottle of 100- 300 mg tabs. They were very euphoric and would make you feel great. But after about 3 hrs when they started wearing off you would feel drunk, like on alcohol. It was dangerous to drive a car. They gave you extreme confidence. So you thought you were ok. But your speech would start to get slurred. And you often started acting like a jerk. Thinking you were the life of the party. Also you would gain a tolerance pretty quickly. So you ended up doing 3-4 tabs to feel the same effects after a few months. Then you would crash and go into a deep sleep. You would wake up about 7-8 hrs a later, realizing you had wrecked your car, left the scene of the accident. Turned off a few girls by being a jerk. Or wake up next to a girl. Where you didn't have sex, you simply both passed out. So even though they made you feel fantastic the first 2-3 hrs. It really had a price to pay. And often you couldn't remember what happened. So in my wise opinion they are better left alone. There are better meds now [22].
Chronic use of methaqualone causing tolerance	I had been taking 3 or 4 a day for about a week, and I was not feeling them like I had been. So I decided to up my dose. Big mistake! I was nodding at the resteraunt and it was a good hour before I was steady on my feet again. The dose could have been as much as 1200 mgs, but was more likely 900-1000 mgs. I will not take more than one at a time and go anywhere in public again. [...] Since there are not many Quaaludes on the street, I don't think too many people will have problems. Be careful! Stick to one 400 mg dose, and don't drink more than one or two drinks (NORMAL DRINKS LIKE A BEER OR SOMETHING WITH ONE OUNCE OF ALCOHOL IN IT) [19].
Symptoms experienced as a result of taking a high dose of SL-164	Doseage: 900-1200 mgs (3-4 Capsules at once). Effects: Subject began to experience typical barbiturate like behaviors, boisterous belligerent behavior. After 45 minutes subject had zero motor function, falling unable to stand or walk severe tremors and shaking present. Subject uncomfortable but refuses medical care. Subject requests cocaine and insufflated one "rail" shaking and tremors stop instantly [51].
Experienced side effects due to the intake of SL-164	This substance has stunning effects; however, it pertains to an awful side-effect: fidgety legs, hands, arms... this continuous sensation of having to move these body parts. Difficulties with typing, dropping items like there's no tomorrow. From my experience, even low doses will produce the same effect if re-dosed. Almost akin to the restless-leg syndrome, although amplified 100x. [...] The effects of the compound, reflecting upon the mental impacts, are very delightful. Better than Soma, comparable to GHB [52]
Awareness of the mutagenic effects of nitromethaqualone and the expressed need for some novel analogues	Except it's a very nice little carcinogen... Possibly the best derivative of Methaqualone and it causes cancer. All the derivatives have one caveat or another. Methaqualone itself seems to be a divinely engineered molecule. All the stuff that's "close to it", even if off by a little bit, have horrible side effects. It's sad [47].
Resistance to discontinuing nitromethaqualone use despite awareness of its mutagenic properties	The thing is, it does have a carcinogenic and hepatotoxic metabolite, but you need much more of the metabolite for it to be toxic, than what gets created when you use the drug. All in all, using it few times should be fine, regularly could be a bad idea [53].
Experience of route-dependent effects induced by mebroqualone intake	Mebroqualone is probably my favorite sedative. when you smoke it, it only lasts like a half hour so it's perfect to pull you back from a stim psychosis freakout or teetering on the edge of a bad trip without ending your night, but orally it lasts like 6 hours so also works as a recreational sedative or sleep aid [54].
Addictive potential of mebroqualone and risk of multi-dosing resulting in loss of control and memory	You can snort it. I did bumps from a 250mg bag over the course of a night and woke up the next day with a large amount of time missing (though i mixed with a little alcohol) [...] whenever i've taken it i've continued taking it until my memory of everything bar the first couple doses is gone. I know of one night I took around 300mg over the course of 6 hours and woke up after about 9 hours sleep with no hangover but a little bit of a groggy feeling that some caffeine sorted [55].

Experiences described on online forums by users	Quote
Effects of mebroqualone when smoked	The standout feature of this drug is definetly the euporic rush when smoked. It produced a very pleasurable euphoric rush that last for about a minute. The rush is sedating and very dis-coordinating and a little bit disassociating. Definitely want to be seated during this. The rush tapers down quickly into a mild benzo like high for the next hour. A reduction in inhibitions and some mild music enhancement. The drug is definitely very fiendish because the rush is very euphoric and short lived [35].
Potentiation of effects due to simultaneous use of mebroqualone with other sedative drugs	Sometimes I have smoked mebroqualone while also having taken my daily etizolam dose and the effect felt was multiplied exponentially. I would literally collapse after exhalation and end up passed out with mysterious wounds and bruises most likely due to my legs giving out and collapsing [56].
Experienced side effects due to the intake of methylmethaqualone	The buzz is somwhat like that of ketamine and a low dose of salvia. I'm getting a wierd pulsating like feeling every half second which is affecting my vision.. Almost like the eye twitching from high doses of amphetamine substances, but it was of a different nature. My hands are twitching a lot.. [57].
Addictive potential of methylmethaqualone and risk of multi-dosing	This is a very strangesdr and uniwue suubstance ei aplogize for the bbad sopelling my body is still twitchthing intensesly.. Alhough it doesnt give really nice effects I still feel the need to dose again as soon as it wears off.. It is very addictive (exactly the same way NOS [nitrous oxide] is - when it wears off you really want it again but just for a few minutes) [57].
Potentiating effect of simultaneous use of ethanol and methylmethaqualone	I had drank a lot of alcohol today, when I arrived home I was still feeling the mental cloudiness but didn't feel 'drunk' Once again I tried smoking 5mg of quack.. After the seizure-like effects I felt amazing.. A great sense of euphoria.. It had brilliant synergistic effects with the low dose of alcohol in my blood (DON'T TRY THIS YOURSELF - ITS DANGEROUS AND I WAS WRECKLESS). Gotta say that has definitely sparked my interest in the substance.. The feeling I felt was beyond euphoria, beyond words.. It was almost a ++++ on the shulgin scale. [...] That was one of the best times I've had experimenting with psychoactive compounds [57].
Planning anticonvulsant drug use to reduce methylmethaqualone side effects	There seems to be a love hate relation ship with this chemical. Roa is divided and it can either be a dud or almost and some times give seizures. What I'd you took antconvolsents with it? I have gabapentin, pregabalin, Phenytoin/Dilantin, Topiramate/Topamax, levetiracetam (Keppra) and I'm tapering flubromazolam. Also tapering bupe a ahalf mg currently. What is the best Roa and do you think these drugs can control the sezure threshold to make this a usable drug an reach higher doses safely [48]?
Convulsion-inducing effects of methylmethaqualone	Just wanted to drop in and reiterate what others have said. Smoking methylmethaqualone will give you convulsions/seizures. I was aware that this was a possible side effect but was experimenting for myself anyways. I had at least one convulsive episode last night while smoking it. Could've been more but I was alone for most of the time so nobody was there to see it except for that one time. TBH, it didn't feel bad but it is a little scary. I'm done with methylmethaqualone [58].
High doses used in the oral intake of etaqualone to achieve the desired effect	I found oral dosing to be enjoyable up until 800mg, after which it felt redundant and, again, I felt as though I had hit some kind of restrictive (and frustrating) cap. Etaqualone appears to be disappointingly inefficient via oral administration; subjectively, enjoyable dosages range from just lower than 500mg to over a gram or more per person, per event. Compared with other routes of administration, oral represents the soundest way to avoid compulsive dosing but overall being the least enjoyable level of exposure to the drug's CNS effects [59].
Strong effects when smoking etaqualone combined with the desire for repeated dosing	Overall, etaqualone was not unworthy. I did, I admit, succumb to the compulsive re-dosing seen with smoking the material. Initially, this feeling was unfamiliar and exciting, if not also unsettlingly powerful. After five to seven hits, my mind felt as though it has struck its cap. I could not re-achieve the rush without waiting to re-dose until I was at the point of fiending for the feeling. This was off-putting. Etaqualone is an insidious creature. Rapid stimulation of the reward system, a unique pleasure that defies logic, re-dose-provokingly short duration of action and multi-variate drug interaction concerns, coupled with dosing that is wholly inconsistent from person to person (anecdotally) are some of the prevalent neurological traits that define etaqualone as a subjective and little-studied human experience. I should also add that smoking etaqualone, with repetition, brings long-lasting irritation to the lungs. I have had coughing symptoms and mucous production - at varying degrees of intensity - for the two weeks it has now been since I last used etaqualone. Smoking etaqualone is an extremely effective ROA with a fast onset (~10 seconds) an a short duration (15-25 minutes full effect; 40 minutes afterglow). This ROA is most likely to unlock the addictive danger of etaqualone as it promotes continuous, compulsive re-dosing despite the diminishing intensity and subjective pleasure of the experience. If one so chooses, my suggestion is to be very careful and wary of re-dosing past your body's physiological limits [59].
Addictive potential of methaqualone derivatives	I'll start off with saying I have smoked/vaped quite large quantities of etaqualone and mebroqualone, but maybe only a gram of methyl-methaqualone in my lifetime. By large quantities I shamefully mean about an ounce of both. The only reason I have smoked so much of these chemicals is because of their rapid onset(rush) and short duration, creating a non stop urge to smoke some more. [...] But the downsides like passing out while standing never stopped me from wanting more, always more more more. The effects I get from smoking mebroqualone are so pleasurable and so sedating, it is like the anti-crack. Some may just find it tiring and boring but if you REALLY wanted to be sedated INSTANTLY [...] mebroqualone is your drug [56].

had consumed SL-164 and opium poppy tea was admitted to a poisoning treatment center in Germany in 2019 with myoclonic convulsions, mydriasis, tachycardia, and altered mental status. The symptoms resolved completely after 72 hours, and the patient reported that he had consumed 300 mg of SL-164, with previous doses of 100 and 200 mg having failed to produce the desired effects [7]. In the second case, a 21-year-old man in the United States presented to the emergency department claiming to have consumed 500 mg of cocaine and 600 mg of methaqualone. However, laboratory analysis revealed that the substance he had taken was SL-164 [13]. The poisoning caused drowsiness, myoclonic jerking, hyperreflection, and methemoglobinemia-induced hypoxia. The authors of this report suspect that the likely cause of methemoglobinemia was contamination present in the cocaine. In their study, adding an SL-164 capsule to a full-blood specimen did not cause an increase in methemoglobin levels. However, the previously mentioned precursor, 4-chloro-o-toluidine, as an aromatic amine, undergoes metabolic activation to form a substance that induces methemoglobin formation. The influence of metabolism on the methemoglobin-forming potential of the precursor may explain the potentially false negative result obtained by Lund et al [13,30]. Additionally, individual reports from users claim that taking SL-164 resulted in methemoglobinemia and the presence of blood in their urine, which supports the notion that illicit SL-164 products possess dangerous methemoglobin-inducing properties [28,29].

Nitromethaqualone (NMQ)

Nitromethaqualone (2-methyl-3-(2-methoxy-4-nitrophenyl)-4(3H)-quinazolinone) is a derivative that was introduced into the pharmaceutical market in Europe during the 1960s. This compound is approximately 10 times more potent than methaqualone, however its mutagenic properties led to its withdrawal from the market. In 2018, reports emerged on forums regarding the recreational use of NMQ [31]. Although some discussions on this substance include warnings about its mutagenicity, some users still choose to use it, perhaps due to its perceived effectiveness in producing desirable effects, such as euphoria, anxiolytic effects, and relaxation (Table II). Reported undesirable effects include muscle tremors, dizziness, and loss of consciousness.

Users typically take NMQ orally at a dose of approximately 25 mg (compared to 300 mg for methaqualone). Intranasal administration requires slightly higher doses of around 30-40 mg, which results in the rapid onset of effects after approximately 10 minutes, peaking at around 1 hour, and then declining. Smoking NMQ is generally not recommended by users, but if someone chooses to do so, low doses of around 5 mg are recommended (Table I).

Mebroqualone (MBQ)

Mebroqualone (3-(2-bromophenyl)-2-methylquinazolin-4(3H)-one) is a mono-brominated derivative of methaqualone, which was first synthesized in the 1960s but was never introduced for medical use. In 2013, it was reported in the United Kingdom as a novel psychoactive substance to the European Monitoring Centre for Drugs and Drug Addiction Early Warning System (EMCDDA's EWA) [32]. Threads discussing this compound began to appear around 2012-13 [33,34], and for about six years, it gained moderate interest and regularly appeared in forums with user reports until 2019. After that time, information about the use of this substance became significantly limited for unknown reasons [35,36].

Users have reported that oral and intranasal administration of MBQ is not very effective, and they recommend other routes of administration, such as smoking, inhalation of vapors, less commonly sublingual administration, and occasionally rectal administration. Smoking or inhalation of vapors produces a very rapid and strong effect within a few minutes, lasting for about an hour with physical effects lasting longer than psychological ones (Table I). Users most commonly compare the effects of MBQ to GHB with a strong stimulating and euphoric effect (Table II). High doses of MBQ have been associated with severe lack of coordination, impaired vision, nystagmus, as well as numbness, severe limb and whole-body twitching, and short-term memory impairment [36,37]. Of particular concern is the often-described multiple dosing of MBQ due to its very strong but short-lived effects. Another dangerous phenomenon is the simultaneous use of this substance with other depressants, most commonly alcohol, to enhance its effects (Table II).

In 2021, two cases from 2018 in the US were described where MBQ was detected in biological material [12]. In the first case, a man died in a fire, and MBQ (10,228 ng/ml), lorazepam, oxycodone, and diphenhydramine were detected in his blood. In the second case, MBQ was detected in the blood of a man who had committed suicide by jumping in front of a train, with concentrations of 115 ng/ml, as well as amphetamine and methamphetamine (65 and 535 ng/ml, respectively). Information about the circumstances surrounding these deaths is limited. However, the high concentration of MBQ in the first case may explain the man's failure to evacuate from the fire [12].

Ephinazone

Ephinazone (2-ethyl-3-phenylquinazolin-4-one) is a novel isomer of methaqualone, for which no existing literature is available. The first reported mentions of this substance appeared on forums in 2013 [38,39]. It remains unclear whether this compound was previously known. While this compound has limited popularity among users, individual threads dedicated to experiences with ephinazone have emerged in recent years (2020-2023) [40–42] In 2021, this compound was identified for the first time in Germany and reported to EMCDDA's EWA [1].

Some users have reported little or no effect following oral ingestion and suggest smoking/inhaling vapors in doses ranging

from 20-80 mg to achieve the desired effects. Others have reported that oral doses of around 100-200 mg result in a moderately strong effect (Table I). Users have reported euphoria, drowsiness, anxiolytic effects, increased sociability, as well as disturbed hearing and vision, jaw tension, and dissociation. Interestingly, many users have reported the absence or significantly reduced physical symptoms such as loss of body control, muscle tremors, etc. in comparison to other methaqualone analogues. There are also reports of concurrent alcohol use to enhance the effect.

Methylmethaqualone (MMQ)

Methylmethaqualone (3-(2,4-dimethylphenyl)-2-methylquinazolin-4-one), also known as MMQ, is one of the earliest known, frequently abused, methaqualone analogues, with the first report of its identification in a seized product dating back to 1993 [43]. Although the earliest online forum threads about MMQ date back to 2008, it is possible that this substance was abused earlier [44,45]. Recent years have also seen reports describing the use of MMQ [46,47].

Among all methaqualone analogues, MMQ is one of the most frequently discussed on online forums. When taken orally, the compound acts in a manner similar to methaqualone, but with slightly lower oral doses, averaging 100-150 mg. The effect of oral intake lasts for 3-6 hours, and taking it on a full stomach results in a significantly weaker effect. Particularly potent effects are described when MMQ is smoked or vaporized. Effective doses ranging from 1 to 25 mg cause intense intoxication lasting several minutes. Other administration routes, such as intranasal and rectal, are occasionally mentioned (Table I).

The most commonly reported effects of MMQ are sedation, euphoria, relaxation, but also loss of coordination and tunnel vision. In cases of severe intoxication, especially when smoked or vaporized, it can cause strong convulsions, short-term memory loss, and severe physical impairment. Some users indicate that the recreational dose is very close to the dose causing overdose resulting in convulsions. The occurrence of convulsions is alarming, and users warn each other against using high doses or multiple dosing that can cause severe and dangerous intoxication (Table II). What is particularly alarming is that some users consider concurrent use of drugs, such as benzodiazepines, to prevent seizures [48]. Another concern among users is the ease of developing an addiction, particularly when smoking or vaporizing.

There is a single reported case of MMQ poisoning in the literature [14]. In 2012, a 24-year-old man in Switzerland was admitted to the emergency department after taking two 500 mg MMQ tablets. The patient exhibited symptoms such as central nervous system depression, psychomotor agitation, muscle overactivity, and tachycardia. The patient was readmitted a few days later after taking the same dose of MMQ again, which is consistent with the suggested addictive potential of MMQ [14].

Etaqualone (ETQ)

Etaqualone (3-(2-ethylphenyl)-2-methyl-quinazolin-4-one) is an ethyl derivative of methaqualone, first synthesized in the 1960s. While it was previously prescribed for insomnia in some European countries, it is currently used as a sedative in China and is abused in many countries [8,10]. The first mentions of its recreational use on online forums date back to 2008, but it is possible that it was being abused even earlier [49]. In 2009, it was reported as a new psychoactive substance (NPS) in Denmark to the EMCDDA [50]. Since then, ETQ has been sporadically mentioned as a used substance among online forum users.

The effects of taking ETQ are most commonly compared to those of methaqualone, but they are reported to be weaker and shorter lasting. Users most frequently describe two routes of administration: oral and smoking/inhaling vapors. Oral doses used are slightly higher than those for methaqualone, with an average dose of about 300-400 mg. Smoking/inhaling vapors are taken with doses averaging 30-80 mg. However, users report that oral ingestion is often ineffective, even at high doses (>400 mg) (Table I). There are also individual reports of intranasal and rectal administration, but these were not preferred due to their irritating effect on the mucous membrane. The strongest effect is achieved when smoking/vaporizing, and the resulting effects include euphoria, sedation, relaxation, hearing and visual disturbances, impaired motor control, and short-term memory disruption. Some users compare the effects of ETQ to drugs such as gabapentin, baclofen, and alprazolam. Due to the short-lived and intense effects resulting from smoking, multiple dosing is common, and users also note a strong addictive potential of this compound (Table II).

Recently, ETQ has begun to replace methaqualone in the commonly used illegal drug called “Huyouyou” in some regions of China [8,10]. Another previously unknown analogue, 2-methoxyqualone (3-(2-methoxypheny)-2-methyl-4-quinazolinone), has also been detected by Yang et al. in this product [9,11]. However, it appears that users are not yet aware of its existence as we found no mention on online forums of this derivative.

Concluding remarks

The illicit market of novel psychoactive substances is continuously evolving, and the challenge of addressing the growing popularity of methaqualone and its analogues may become increasingly difficult in the future. Although threads on methaqualone analogues were considerably less frequent than those related to methaqualone itself, the occurrence of analogue use appears significantly alarming. Their preparations are often adulterated with harmful by-products, and most of the analogues we have described, with the exception of ETQ, show greater potency, reflected in the lower doses required to produce an effect. The most prominent in this respect, NMQ, exhibits about 10 times the potency of methaqualone. Even more alarming are indications that the effective doses used

for most of the analogues are simultaneously doses that commonly induce severe adverse effects, particularly in the form of severe convulsions, loss of motor control and unconsciousness. Therefore, the use of methaqualone analogues is always associated with risk as there is no safe dosage for them. The potential for dangerous side-effects is even greater when other depressants are taken concurrently; indeed, users most commonly describe potentiating effects when alcohol is taken simultaneously.

Another interesting phenomenon that can be observed is the repeating cycle for many analogues. Initially, a substance gains popularity and extensive interest in it is expressed, at which point threads appear with questions and requests regarding details of experiences with the substance. Subsequently, threads describing experiences, including the negative ones, become popular, and then interest in the substance seems to decline, with emerging threads consisting mainly of warnings. A situation like this was exactly the case with the threads on SL-164 and nowadays if posts or comments appear on it, they mainly contain warnings. Apart from the analogues described in this article, many other compounds were synthesized in the past as potential drugs, and some have even found use in the pharmaceutical market [5]. These compounds may also begin to appear on the illicit substance market in the future. However, as the recent example of 2-methoxyqualone demonstrates, it is also possible for completely new, previously unknown compounds to appear on the market [9,11].

Toxicological information on methaqualone derivatives is limited, and sources in the form of reports from online forums by users are extremely valuable, especially in the absence of more reliable sources of information. Nevertheless, caution should be exercised when using such data for several reasons. Firstly, users can never be sure of the specific substance they are taking and its purity, thus their reported experiences may be the result of taking other substances or even mixtures of substances, which may inadvertently falsify their descriptions. Additionally, the concentration and purity of the substances they are taking may vary, resulting in different symptoms of poisoning and different effective doses. In addition, reported effects may be intentionally inaccurate, for instance in order to promote a specific substance. Furthermore, forums may not reflect the global situation, but only local specifics. Nevertheless, these sources, especially when treated carefully, may prove useful and serve as a partial substitute for toxicological data in the absence of more reliable sources.

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