Rediscovering MDMA (ecstasy): the role of the American chemist Alexander T. Shulgin

Udo Benzenhöfer & Torsten Passie
Senckenberg Institute for the History and Ethics of Medicine, University of Frankfurt/Main, Frankfurt/Main, Germany and Department of Psychiatry, Social Psychiatry and Psychotherapy, Hannover Medical School, Hannover, Germany

ABSTRACT

Aims Alexander T. Shulgin is widely thought of as the ‘father’ of +/−3,4-methylenedioxymethamphetamine (MDMA). This paper re-assesses his role in the modern history of this drug. Methods We analysed systematically Shulgin’s original publications on MDMA, his publications on the history of MDMA and his laboratory notebook. Results According to Shulgin’s book PIHKAL (1991), he synthesized MDMA in 1965, but did not try it. In the 1960s Shulgin also synthesized MDMA-related compounds such as 3,4-methylenedioxyamphetamine (MDA), 3-methoxy-4,5-methylenedioxyamphetamine (MMDA) and 3,4-methylenedioxyethylamphetamine (MDE), but this had no impact on his rediscovery of MDMA. In the mid-1970s Shulgin learned of a ‘special effect’ caused by MDMA, whereupon he re-synthesized it and tried it himself in September 1976, as confirmed by his laboratory notebook. In 1977 he gave MDMA to Leo Zeff PhD, who used it as an adjunct to psychotherapy and introduced it to other psychotherapists. Conclusion Shulgin was not the first to synthesize MDMA, but he played an important role in its history. It seems plausible that he was so impressed by its effects that he introduced it to psychotherapist Zeff in 1977. This, and the fact that in 1978 he published with David Nichols the first paper on the pharmacological action of MDMA in humans, explains why Shulgin is sometimes (erroneously) called the ‘father’ of MDMA.

Keywords Alexander T. Shulgin, ecstasy, history, MDMA.

INTRODUCTION

Today +/−3,4-methylenedioxymethamphetamine (also known as MDMA or ‘ecstasy’) is a popular, illicit recreational drug. In spite of public opinion, MDMA is not a new substance. It was first synthesized in 1912 by the chemist Arthur Koellisch and was rediscovered more than once between the 1920s and 1960s [1–8]. In the late 1970s and 1980s, it was used occasionally as an adjunct to psychotherapy and increasingly as a recreational drug [1,2,9]. MDMA was placed into Schedule I by the US Drug Enforcement Administration (DEA) in July 1985 by the invocation of the Emergency Scheduling Act and was permanently scheduled on 13 November 1986 [10,11]. Alexander T. Shulgin’s role in the history of MDMA became prominent in 1978 after publishing with medicinal chemist, David Nichols (Purdue University, Indiana), the first report of the psychopharmacological effects of MDMA in humans [12].

Well into the 1990s, Shulgin published not only influential papers on the chemistry and psychopharmacology of MDMA but also on its history; yet Shulgin has offered slightly different versions of his role in the history of MDMA in his 1986, 1990, 1991 and 1997 publications [1,2,13,14]. To come to a clearer understanding of the significance of Shulgin in the public awareness of what is MDMA, it is necessary to take a closer look at these publications and then compare the facts offered with Shulgin’s laboratory notebooks. Nota bene: it is not the aim of this paper to write an overall history of the ‘entactogenic’ drugs.

THE EARLY HISTORY OF MDMA

MDMA was first synthesized in the context of the search for haemostatics at the pharmaceutical company Merck KGaA (of Darmstadt, Germany) in 1912 and patented in
1914 [3,6–8]. The first pre-clinical pharmacological tests with MDMA were performed at Merck in 1927 during searches for adrenaline- or ephedrine-like substances [6,7]. In 1952, a Merck chemist conducted toxicological tests with MDMA [3,6,7]. From 1953 to 1954, the toxic effects of MDMA were studied in five species of laboratory animals at the University of Michigan [1,15]. In 1959, a Merck chemist interested in the production of new stimulants worked with MDMA, but it remains unclear as to whether he evaluated effects in humans [3,6,7]. In 1960, two Polish chemists published a paper describing the synthesis of MDMA as an intermediary product [16]. The next phase of MDMA research commenced when Alexander T. Shulgin (Fig. 1) appeared on the stage.

ALEXANDER T. SHULGIN: A BIOGRAPHICAL NOTE

According to papers based on Shulgin’s autobiography and on interviews [17–19], Shulgin’s curriculum vitae can be summarized as follows: born in 1925 in Berkeley, CA, USA. Shulgin pursued studies in chemistry and biochemistry after serving in the US Navy during World War II. He earned a PhD from the University of California at Berkeley in 1955. In 1955, while working at Dow Chemical Company in Walnut Creek, CA, he had his first experience with the hallucinogen mescaline, which was not illegal at that time. Two years later he created one of the world’s first biodegradable insecticides for Dow Chemical. In return, Dow Chemical gave him the freedom to study whatever interested him. Shulgin turned towards discovering psychoactive drugs.

He synthesized and tested the effects of more than 200 potentially psychoactive substances, often by taking them himself or with a close circle of collaborators [13,20]. Eventually Dow Chemical was disappointed at having its address noted on these Shulgin publications. In 1966, Shulgin left Dow Chemical to work as a research chemist and consultant. In his private laboratory at Lafayette, CA, he continued to develop psychoactive drugs, among them many new psychedelic phenethylamines, amphetamines and tryptamines. During this time Shulgin received a Schedule I registration for research and cooperated with the DEA. In 1991, together with his second wife Ann, he published PIKHAL (Phenethylamines I Have Known And Loved), a fictionalized autobiographical work with an appendix describing the synthesis and effects of 179 phenethylamines [13]. In the early 1990s, Shulgin relinquished his Schedule I license. In 1993, the DEA raided his laboratory. There were no Scheduled substances found during the incident, and no charges were filed. In his continuing work, Dr Shulgin has scrupulously avoided synthesis of controlled substances [18,19], and continues legitimate research in collaboration with scientists at many institutions worldwide.

ON THE POSSIBLE ROLE OF MDA, MMDA AND MDE IN THE HISTORY OF THE REDISCOVERY OF MDMA

3,4-Methylenedioxyamphetamine (MDA), 3-methoxy-4,5-methylenedioxyamphetamine (MMDA) and especially 3,4-methylenedioxyethylamphetamine (MDE) are substances which have a great similarity to MDMA. Their possible role in Shulgin’s discovery of the psychotomimetic effects of MDMA will be discussed here.

MDA was first synthesized in 1910 [21]. Pre-clinical tests by the US military were completed in the mid-1950s [15]. Early trials as an antidepressant and anorexic agent produced inconclusive results [22]. The psychopharmacological effects of MDA in humans were described by Alles in 1959 [23]. Shulgin, most probably following Alles’ research, synthesized MDA in May 1961 [24]. He tried it in May 1961 at a small (inactive) dose [4.5 mg per os (p.o.)] [24] and again in August 1965 at small (inactive) doses (15.2–35 mg p.o.) with ‘no effect’ [24].


During the mid-1960s, Shulgin initiated tests on the psychotherapeutic potential of MDA and MMDA with psychotherapist Claudio Naranjo MD at the Department of Anthropological Medicine, University of Chile (Santiago de Chile) [27,28]. The results were favourable and were published in 1967 on MDA [29] and in 1973 on MMDA [28,30].
Shulgin, according to PHIKAL, synthesized MDMA in 1965 [13]. We have found no evidence for that in his laboratory notebooks (see below) but, of course, nor can we disprove this statement. Regardless, Shulgin did not perform self-trials with MDMA in the 1960s. One could have expected that if he had come to synthesize it as a result of a planned research line regarding the intoxicating effects of the methylenedioxy compounds, then he would have performed his usual self-trials.

In 1967, Shulgin mentioned in his laboratory notebook 3,4-methylenedioxyethylamphetamine (MDE), a new compound almost identical chemically with MDMA. There is only a very short notice about MDE contained in his laboratory book in which he described how he was informed in June 1967 by a certain ‘KOZ’ (pseudonym for Claudio Naranjo MD) that 100 mg MDE produced ‘N.R. (= no reaction)’ [31] (MDE is psychoactive above 130 mg). It may be speculated that because of Naranjo’s report, Shulgin did not test MDE (and related compounds such as MDMA) himself during the next few years.

It is evident, then, that Shulgin’s interest in methylenedioxy compounds brought him very close to MDMA during the 1960s (we have to leave open if he actually synthesized it in 1965), but he did not realize its special effects during that time.

**SHULGIN ON THE HISTORY OF MDMA**

In 1978, Shulgin, together with medicinal chemist David Nichols, published a paper dealing with the effects of MDMA in humans [12]. This paper goes back to a presentation Shulgin gave in late December 1976 at a conference entitled ‘The psychopharmacology of hallucinogens’ in Bethesda, MD. The authors erroneously attribute the first synthesis of MDMA in 1960 to the Polish chemists Biniecki & Krajewski [16]. Shulgin & Nichols wrote that, according to a paper by Gaston & Rasnussen [32] and a personal communication by C. Helisten from the PharmChem Foundation at Palo Alto, MDMA had made an occasional appearance on the illicit street-drug market in 1970. The description of the ‘psychotomimetic’ effects of MDMA in this paper is very brief: ‘Qualitatively, the drug appears to evoke an easily controlled altered state of consciousness with emotional and sensual overtones. It can be compared in its effect to marijuana, to psilocybin devoid of the hallucinatory component, or to low levels of MDA’ [12].

In 1986, Shulgin described the background and chemistry of MDMA in a special paper [1]. Shulgin had conducted his historiographical homework and now paid tribute to the first synthesis of MDMA at Merck KGaA in 1912. In this publication Shulgin referred to a large study of the toxic effects of MDMA in animals performed at the University of Michigan under a classified contract with the US Army (Chemical Corps, Edgewood Arsenal, MD). The study by Hardman et al. had been performed during the 1953–54 period, declassified in 1969 and published in 1973 [15]. Shulgin also mentioned recent studies on MDMA as an adjunct psychotherapy, but did not give any hint regarding his own role in ‘initiating’ the psychotherapist, who was then responsible for introducing MDMA to many other psychotherapists in the United States (this was revealed in Shulgin & Shulgin [13], see below, and by Stolaroff [33]).

In 1990, Shulgin wrote a comprehensive ‘history of MDMA’ [2]. He mentioned the Merck initial synthesis (1912), the Merck patent (1914), another Merck patent from 1920 describing a chemical modification of MDMA, and the work of the Polish chemists Biniecki & Krajewski [16]. According to this study, the first reports that MDMA was becoming available on the street were published in 1972 [32], with observations from 1970 in Illinois and Indiana [34]. According to Shulgin’s 1990 paper [2], MDMA was first introduced into clinical practice (no names were given) on the West Coast in the latter part of 1976 and was used by therapists on the East Coast a few months later [35]. In this paper, Shulgin’s role was reduced to the fact that, together with David Nichols, he had published the first paper on the pharmacological action of MDMA in humans in 1978.

The first part of Shulgin’s book PIKHAL [13] is autobiographical. Shulgin’s ‘alter ego’ in PIKHAL is called ‘Shura’. In his book Shulgin gave the first detailed account of how he rediscovered MDMA. He wrote on p. 69 of the book: ‘In fact I had synthesized it [= MDMA] back at Dole [= Dow Chemical] in 1965’. However, according to Shura/Shulgin, he had not tried it then and had forgotten about it until the 1970s. We should insert here that we have no reason to doubt Shulgin’s statement about his synthesis of MDMA in 1965, but we should mention that we could not find proof for it in his laboratory notebook (see below). According to PIKHAL, the story continues as follows: Shura/Shulgin met a young professor of chemistry called ‘Noel Chestnut’ in 1967. It must have been some years later, although no date is given, that while ‘Chestnut’ held lecture tours in other parts of the world Shura/Shulgin was made ‘daddy-in-residence’ for ‘Chestnut’s’ graduate students in San Francisco. Shulgin wrote (still on p. 69): ‘One of these was a dear, dear sprite appropriately named Merrie Kleinman, who told me that she had done an experiment with two close friends of hers, and that they had used 100 milligrams of N-methylated MDA (MDMA). She shared very little about the experience, but implied that it was quite emotional, and that there had been a basically good reaction from all three of them’. Shulgin then reported the experiences of other people with MDMA he had heard of at that time and mentioned that he himself had taken...
MDMA a little later, together with other people (without revealing the exact time). He finally revealed that in 1977 he had introduced MDMA to a retired psychologist in Oakland, CA. According to Shura/Shulgin, this psychologist (pseudonym: Adam Fisher; later identified as Leo Zeff [13]) was so impressed by the effects of MDMA that he abandoned retirement and introduced MDMA to many psychotherapists across the United States [13].

Even more details (and slightly different ones) are offered in Shulgin’s German-only paper of 1997 [14]. Shulgin wrote that in about 1970 he had sent a letter to a chemist, who was the founder of a chemical company in Los Angeles. The chemist had asked for instructions on how to prepare N-methylated MDA (MDMA). Shulgin sent him the instructions on how to make MDMA via the conversion of MDA to the formamide that is reduced with lithium aluminium hydride. According to a letter Shulgin received from the chemist a little later, the chemist had provided access to this information to one of his ‘clients’ who studied psychology in the Midwest. Perhaps Shulgin mentions this because (although this is only speculation) he had the notion that his ‘instruction’ had led to the appearance of MDMA on the streets in some cities in the Midwest in the early 1970s [34].

Another new detail is revealed in this paper: Shulgin wrote that he had first heard of the special effects of MDMA from a young student ‘in around 1975’. According to Shulgin, the student (no name is given) was the brother of a dentist who had paid a visit to San Francisco. He had told Shulgin that he had read a publication by Shulgin on ‘2C-D’ (2,5-dimethoxy-4-methyl-phenethylamine) and ‘2C-B’ (4-bromo-2,5-dimethoxyphenethylamine) and that he had taken some ‘N-methyls’, especially N-methylated MDA (=MDMA), which had an ‘amphetamine-like content’. According to the paper from 1997 the next mention of MDMA (in the middle of the year 1976) came from a female student who had taken 100 mg of MDMA together with two friends. This student had been named as ‘Merrie Kleinman’ in PIKHAL. Shulgin then mentions a colleague from the University of San Francisco who had synthesized and taken MDMA. Shulgin finally reveals that he took MDMA for the first time in September 1976 (which is confirmed by his laboratory notebook; see below).

**MDMA IN SHULGIN’S LABORATORY NOTEBOOK**

The most reliable sources for Shulgin’s history with MDMA are his laboratory notebooks. The first of these books (started in 1960) was made accessible in 2007 via the internet [24]. It is important to realize that two of Shulgin’s assistants have erased the names of most people mentioned in the notebook and have inserted pseudonyms such as Marty, Fredo, etc. To read Shulgin’s entries regarding MDMA correctly, it is important to note that the notebook had not been kept on a day-to-day basis. Often Shulgin began a new page with the description of a new substance and later completed notes regarding the time before and—more often—the time after the synthesis or the first trial.

The context of p. 186 (cf. Fig. 2), where he recorded his first trials with MDMA, makes clear that the page was begun in 1976, although the first two entries refer to 1975. These two entries beginning with ‘~’ were obviously recording what he remembered.

The first ‘~’-entry is: ‘~1975: Marty—reports considerable amphetamine-like content’. It is evident that ‘Marty’ is identical with ‘the brother of a dentist’ mentioned in Shulgin’s paper from 1997.

The second ‘~’-entry concerns the graduate student mentioned in PIKHAL [13] (‘Merrie Kleinman’) and in Shulgin’s publication of 1997 (anonymous): ‘~5/30/1976: 100 mg Fredo (+ 2) Rapid onset in ~1 h—lasts to 3 then drops off quickly—mydriasis persists to 4 h. Emotional experience and basically good reaction by all three—little detail’ (p. 186). Directly above the ‘(+ 2)’ Shulgin had drawn a downward-pointing arrow. The text that follows explains: ‘2 other people, not ++ in scale of +4—one is Amos I think’ (p. 186).

In a box on the right-hand side of p. 186 (it is unclear when Shulgin added it), the trials of a certain ‘Flip’ with ‘N-methyls’, especially with ‘N-methylated MDA (=MDMA)’ are listed.

‘Flip’ had taken 15, 30, 45, 60, 75, 100 and 150 mg of MDMA. Up to 60 mg the result was ‘no effect’: 75 mg made him ‘fuzzy’, 100 mg and 150 mg made him ‘active’. It is obvious that ‘Flip’, who is with certainty identical with the unnamed colleague mentioned in Shulgin’s paper from 1997 who had then tried some tri-methoxymethamphetamine, had performed a relatively systematic self-trial with MDMA before Shulgin.

In the same box there is a short entry about a certain ‘C. B.’, who took either 75 or 175 (not completely legible) mg of something (most probably MDMA). The result was ‘fine control’.

The entries that record the first series of trials of Shulgin himself are listed on the left-hand side of p. 186. The context of their importance, these entries will be cited in full (ATS stands for Alexander T. Shulgin; n. e. stands for no effect; ASC stands for altered state of consciousness):

- 9/8/76: 16 mg ATS 11:30 AM. n. e.
- 9/9/76: 25 mg ATS 2:20 AM. n. e.
- 9/12/76: 40 mg ATS 2:35 PM. n. e.
- 9/17/76: 60 mg ATS 12 noon n. e.
5/10/76, 100 mg ATS 10:00 AM [0:35] first awareness—smooth—very nice—I will be attentive to sensory changes (there are none)—looking forward with interest. I can and do quickly accommodate to this ASC. [0:45] still developing—but I can easily assimilate it as it comes. Under excellent control. [0:50] getting quite deep but I am keeping apace. [1:00] well into it—but I am accommodated—piano went well—lots of time to search

Figure 2 Reproduction of p. 186 of Shulgin’s original laboratory notebook referencing to MDMA. Courtesy of Alexander T. Shulgin
out correct notes—no mydriasis—no physical tox. [1:30]
100 → 50% starting to clear. [1:45] trial erot., ejac.
Fine—rapid recovery—[2:15] → 5% I am substantially
out. [3:00] all out. I will try 125.
10/23/76, 100 mg ATS (3:52 P.M. = [0:00]) [0:27]
first slight hint [0:30] start [0:35] roll of eyes with a bit of
erotic init. 15%—I might have said ‘I feel that drink’
[0:45] at 40% I don’t think I am suppressing it—a real
40% [0:49] time slowed? [0:57] largely window (80%)
[1:00] a little dilution. [1:03] complete window—
complete control nonetheless [1:12] holding steady
[1:25] Easy erotic—no need (ability?) of erection [1:50]
dropping? [2:10] down to 50% sex with Nina (6 P.M.)
extraordinarily pleasant—she turned on too! (this was
my return day from Washington) [2:49] a few % left
[3:00] out.

The entries make clear that Shulgin performed his first
self-experiments with MDMA in September/October
1976 in a systematic manner. They tell us that he was
quite impressed by the effect so he continued his trials,
as shown by a remark at the bottom of p. 186 of the
notebook.

CONCLUSION

In the 1960s Alexander T. Shulgin conducted extensive
research on methylenedioxy compounds (i.e. MDA, MDE,
MDMA). This brought him very close to the synthesis
of MDMA, but we have found no proof that he synthesized
MDMA while following this research line at that time.
Shulgin played an important role in the history of
MDMA, especially so during the 1980s and into the
1990s, when the psychoactive effects of this drug were
popularized. A closer look at his early descriptions (1978,
1986 and even 1990) [1,2,12] reveals how he initially
minimized his role in the history of MDMA, most prob-
ably because he wanted to protect his privacy. The first
time he published an almost complete account was in his

Shulgin’s best account appears in his German-
language paper of 1997 [14]. On the basis of his labora-
tory notebook, now available via the internet, we could
verify some of his published details. Shulgin’s laboratory
notebook, for example, confirms the important fact that
in 1975 Shulgin had first heard about a special effect
caused by MDMA. Of greatest significance is the labora-
tory notebook entries of Shulgin performing his first self-
trials with MDMA in September/October 1976 [27]. The
first report on MDMA was given at a conference in
December 1976 and then published in 1978 [12]. In
1978 two other publications [36,37] and a conference
presentation [38] by Shulgin and his coworkers described
the effects of MDMA in more detail, and contributed sig-
ificantly to the distribution of knowledge about it (see
also [39]). There is no evidence so far that Shulgin was led
by his own lines of research to the synthesis of MDMA,
even in spite of the fact that he synthesized some closely
related substances during the 1960s.

In summary, Shulgin played a major role in the
history of MDMA since 1975/76. He was, as far as we
know, the first to perform systematic self-trials with it
(1975/76), he was the first to speak at a scientific confer-
ence (1976) and to publish (1978) on its ‘psychotomi-
metic effects’, as he called it, in humans. He also played a
major role in its history by introducing MDMA to Leo Zeff
PhD, who propagated it as an adjunct for psychotherapy.

Declarations of interest

The authors have no conflicts of interest and are not in
any way connected to industry or any company.

Acknowledgement

Grateful thanks are extended to Alexander T. Shulgin
PhD and Paul F. Daley PhD of the ASRI, Lafayette, CA,
USA, for helpful comments on the manuscript.

References

1. Shulgin A. T. The background and chemistry of MDMA. J
Ecstasy: The Clinical, Pharmacological and Neurotoxicological
Effects of the Drug MDMA. Boston: Kluwer Academic Pub-
Bewußtseinsforsch 1997/1998 [printed 2000]: 6/7:
95–125.
4. Pentney A. R. An exploration of the history and controver-
sies surrounding MDMA and MDA. J Psychoact Drugs 2001;
33: 213–21.
5. Parrott A. C. Is ecstasy MDMA? A review of the proportion
of ecstasy tablets containing MDMA, their dosage levels,
and the changing perceptions of purity. Psychopharmacol-
6. Bernschneider-Reif S., Öxler E., Freudenmann R. W. The
origin of MDMA (‘Ecstasy’)—separating the facts from the
7. Freudenmann R. W., Öxler E., Bernschneider-Reif S. The
origin of MDMA (ecstasy) revisited: the true story recon-
structed from the original documents. Addiction 2006; 101:
1241–5.
8. Benzenhöfer U., Passie T. Wer hat’s entdeckt? Zur Fruehge-
In: Inciardi J. A., editor. Handbook of Drug Control in the
11. Doblin R. E. Regulation of the medical use of psychedelics
and marijuana. Dissertation, Cambridge, MA: Harvard Uni-


