

Drug Facts

Synthetic Cannabinoids

AKA: Fake Canna; Synthetic Cannabinoid Receptor Agonists, SCRA's

Generic slang: Spice, Mamba

Pre-ban products included: Pandora's Box, Exodus, Exodus Damnation, Abyss, Psyclone, Sensate, Clockwork Orange, Magic Dragon, and many others.

Some of the names are similar to strains or forms of cannabis, e.g. *Blue Cheese, White Widow, Green Crack*.

Also referred to as: *Incense, Smoking Mixture, Pot Pourri*.

The drugs in question typically work on **cannabinoid receptors** in the brain and body. They should therefore properly be referred to as **Synthetic Cannabinoid Receptor Agonists (SCRAs)**. Although accurate the term isn't widely used and so the term Synthetic Cannabinoids is used here as it's more understandable to most people.

OVERVIEW: Synthetic cannabinoids have been on the market since around 2008, but for a while their presence hadn't been detected. "Herbal smoking mixtures" such as Spice or Aztec Gold were sold by head-shops and on-line sellers as an alternative to cannabis.

This, in turn was nothing new. Head-shops had, for years been selling "smoking mixtures," usually a mixture of plant material with loosely psychoactive properties. Such mixtures had generally resulted in a headache, sore throat and a house that smelt like an autumnal bonfire. The newer compounds like Spice were different – they actually worked and so interest and use started to increase.

Analysis of samples of Spice revealed that, rather than being a blend of herbal smoking mixtures, the products were actually some inert plant material, which had been sprayed with a **synthetic cannabinoid** – a chemical which mimicked the action of THC or CBD at cannabinoid receptors in the brain.

MECHANISM OF ACTION: THC is one of the naturally-occurring chemicals present in herbal cannabis and cannabis resin. It is involved in the euphoria associated with cannabis use, but may also be involved in less pleasant effects such as panic, paranoia and mental health problems. In 'traditional' strains of cannabis, THC is present alongside other cannabinoids including CBD, which is believed to play an important role in the anxiety-reducing, relaxing effects of cannabis.

THC and CBD bind to and activate **cannabinoid receptors** in the brain – CB1 and CB2 receptors. Synthetic cannabinoids occupy the same receptors. However, they may be far more potent than



“natural” THC – with some synthetics believed to be 100 x the strength of THC. They may also have different affinities – binding more selectively to receptors in one part of the brain or body rather than others.

We don’t know that much about how these newer compounds work. There is some concern that they may also affect other brain chemicals such as serotonin, which may contribute to observed symptoms such as overheating and hallucinations.

LEGAL SITUATION: Novel SCRA’s weren’t covered initially by the Misuse of Drugs Act 1971 (MDA) and so were sold legally via the Internet and “Headshops.”

As compounds started to be sold for recreational use, some were regulated by being added to the list of Controlled Drugs under the MDA.

In 2009 the Naphthoylindoles, Naphthylmethylindoles, Naphthoylpyrroles, Naphthylmethylindenes, Phenylacetylindoles and Cyclohexylphenols became Class B Controlled Drugs.

In 2013 Benzoyl indoles and Tetramethylcyclopropylcarbonyl indoles were also added.

The Psychoactive Substances Act came in to force on 26/5/2016 and covers all remaining SCRA’s. Although not making them Controlled Drugs it made it an offence to produce, import, export or supply any non-exempt psychoactive substances. Possession in custodial settings is also an offence.

Discussion is currently underway with to add all remaining SCRA’s to the Misuse of Drugs Act with a catch-all piece of legislation which would make any substance with action at CB1 receptors a Controlled Drug.ⁱ

ORIGINS: Synthetic cannabinoids were originally developed for use in research settings. They were synthesized by researchers exploring how cannabinoids work on the brain. The first synthetics were developed in the Sixties and Seventies. A huge number were developed in the States in the mid-eighties by John William Huffman. Compounds he developed, such as JWH-018 appeared in the Spice and Aztec Gold smoking mixtures.

Since then many more synthetic cannabinoids have reached the market. The newest products on the market have been around for a very short period of time so little is known about them.

These newer compounds didn’t all emerge from lab research and were developed solely for recreational use.

DRUG FAMILIES include:

Classic cannabinoids: e.g. HU-210, Win-55,212-2

Cyclohexylphenols : e.g. CP-47,497 CP 55-940 (developed by Pfizer in the 70s)

Naphthoyl indoles: e.g. JWH-018, JWH-073, JWH-210 and many others

A list of the family and their relative potential at receptors can be found [here](#).ⁱⁱ

Naphthylmethyleneindenes : e.g. JWH-175

Naphthoylpyrroles: e.g. JWH-370, JWH-346, JWH-244

Phenylacetyl indoles: e.g. JWH-250, JWH-167, JWH-252 and many others;

A list of the family and their relative potential and receptors can be found [here](#).ⁱⁱⁱ

Tetramethylcyclopropylcarbonyl indoles: e.g. UR-144

Benzoyl indoles: e.g. AM-694, AM-1241, AM-2233, RCS-4,

Adamantoyl indoles: e.g. APICA (SDB-001), APINACA (AKB-48)

Naming of synthetic cannabinoids is rather confusing. Some of the chemicals emerged from laboratory research into cannabinoids and so the compounds were given reference codes from research.

For example, a sequence of compounds developed by John William Huffman in America were given the initials JWH, followed by a number (e.g. JWH-018.) HU- compounds were developed by Hebrew University.

Each compound has a long chemical name. Often they have more than one. There is an “official” name based on an international naming standard (IUPAC).

But some drugs end up with unofficial names too, and abbreviations derived from these unofficial names. Then as branded products hit the market, people referred to these instead of chemical names. The example below illustrates this.

Lab-name	Chemical Group	Chemical Name	Brands
JWH-108	Naphthylindoles	1-alkyl-3-(1-naphthoyl)indole	Spice
UR-144	Tetramethylcyclopropylcarbonyl indoles	(1-pentylindol-3-yl)-(2,2,3,3-tetramethylcyclopropyl)methanone	Mary-Joy

With some of the newer compounds the situation is more complex. The drugs didn’t emerge out of laboratory research. They are proper “designer drugs,” designed and intended to work round laws in force at the time.

People naming them copied the lab-style names, but they also gained abbreviated chemical names and brand names.

Take one example, **AKB-48**.

The ‘official’ name is *1-pentyl-N-tricyclo[3.3.1.1^{3,7}]dec-1-yl-1H-indazole-3-carboxamide* but it is also known as *N-(1-adamantyl)-1-pentyl-1H-indazole-3-carboxamide*. This unofficial name led to an abbreviated name of APINACA derived from the long chemical name.

And why AKB-48 in the first instance? Possibly because it was derived from an earlier compound called AB-001. AKB-48 was first reported in Japan in 2012 and there’s a Japanese girl band called AKB-48 so maybe it was named after them.

Examples of the nomenclature for third generation SCRA:

AKB-48	N-(1-adamantyl)-1-pentyl-1H-indazole-3-carboxamide 1-pentyl-N-tricyclo[3.3.1.1 ^{3,7}]dec-1-yl-1H-indazole-3-carboxamide	APINACA
5F-AKB48	N-(adamantan-1-yl)-1-(4-fluorobutyl)-1H-indazole-3-carboxamide	5F-APINACA
PB-22	Quinolin-8-yl 1-pentyl-1H-indole-3-carboxylate	QUPIC
5F-PB22	1-(5-fluoropentyl)-1H-indole-3-carboxylic acid 8-quinolinyl	5F-QUPIC
STS-135	N-(adamantan-1-yl)-1-(5-fluoropentyl)-1H-indole-3-carboxamide	5F-2NEI

APPEARANCE: Synthetic cannabinoids start off in their raw form as crystalline white powder though this is not the most common form at a street level. This is the form in which it is usually imported in to the UK.

This would be very potent and would in turn be mixed with tobacco or another smoking mixture for consumption. There are few reports of attempts being made to snort it or inject it.

More common is for the cannabinoids to be dissolved in a solvent, and sprayed onto an organic herbal material for sale. These will generally be greenish-brown in colour. Some resinous forms may also be available, looking more like cannabis resin.

Prior to the introduction of the Psychoactive Substances Act most of the packaged drugs were then sold in printed foil ziplock packages. Examples of these are pictured at the start of this briefing. There were hundreds of brands on sale prior to the ban.

It was sold in a liquid form suitable for use in E-cigarettes. There is not much evidence that this is widely available post ban.

Post-ban, product is still sold in printed bags. There is also a lot of stock being sold in un-labelled jiffy bags, as left-overs or newly-compounded stock is sold in unbranded forms.

Prisons have also reported SCRA's smuggled in sprayed on to paper, which can then be smoked.

SOURCE: Before the legislative changes raw powder was primarily imported from China. It was made in batches in the UK and sold on-line, via headshops, resold on the streets and smuggled in to prisons.

Post-ban, it is unclear if SCRA's are still being imported in significant quantities. Some of the product currently being sold is probably old stock that pre-dates the ban. Anecdotally powder drugs are still being batched up in the UK so at present there is a mix of old stock and newly-compounded unlabeled stock.

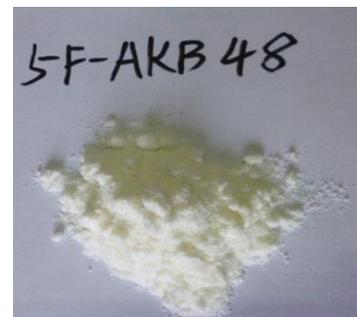
COSTS: Pre-ban SCRA's typically sold for £10/g, £15 3/g.

Since the legal changes prices have gone up significantly with some street agencies saying there's been a 300% increase in costs.

Product in prison is much more expensive, retailing at £50/g or more.

POPULARITY: We don't have clear evidence of levels of SCRA use in the UK. Self-disclosure shows relatively low levels compared to "traditional" cannabis amongst recreational drug users.

Use in the UK seemed to end up concentrated amongst young people attracted by legality and the



erroneous belief it would be safer than normal cannabis.

Elsewhere the main drivers of popularity seemed to be cost and access, especially amongst homeless and vulnerably housed users. Legality and non-detectability were key drivers for use amongst those in criminal justice settings especially in prison where use went up massively.

For some users it was seen as a cheaper, stronger alternative to cannabis. For other users it seems the relationship was more akin to use of an opiate like heroin, using it for the intense euphoria and detachment that it provided.

QUALITY, STRENGTH and DOSES:

When SCRA's first came to market they didn't specify the active chemicals in the mix, and listed instead a range of herbal ingredients, giving the impression that this was responsible for the psychoactive effects.

As branded products were sold more widely in Headshops, Trading Standards were proactive in removing incorrectly-labelled product. In response, manufacturers became more diligent with labelling and more (but not all) branded products were labelled accurately.

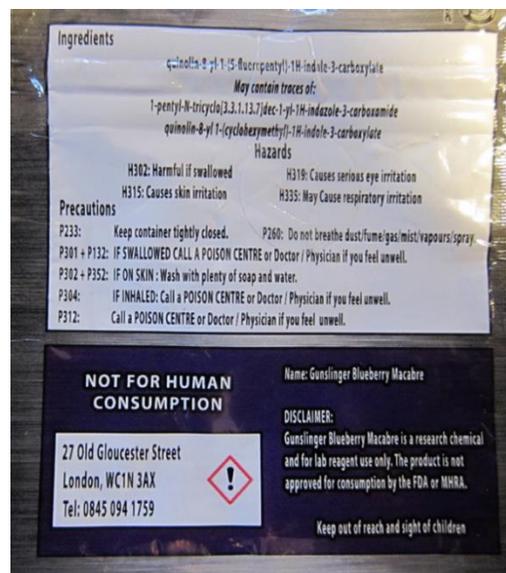
Even when product was correctly labelled, it wouldn't specify the potency of the mix. Depending on how the product was mixed, some were more evenly dosed, and others would have "hot-spots" of concentrated drugs.

When substances were removed from packaging to sell on the streets or in prisons, several different brands could be mixed up making it impossible to know which compounds someone was taking. This situation has become the norm since the Psychoactive Substances Act came in to force, as there is less branded product around and more DIY produced, unlabeled mixture.

So with synthetic cannabinoids the actual composition and strength of any product is an unknown. Products have been analyzed by professional laboratories, and appear on databases such as TicTac or WEDINOS. Such should be treated with caution as they don't reflect the changing nature of the product at a street level.

Analysis of products shows that many branded products contained at least two different psychoactive compounds. Some people find that these substances can be more unpredictable and harder to manage.

Having said this, even if people knew which products they were specifically using, the lack of detailed information about differences between specific products would mean that additional substance-specific harm reduction information would be thin on the ground. We can really only talk in general terms about synthetic cannabinoids at this stage.



Synthetic cannabinoids are often much stronger than their natural counterparts. Starting doses need to be much smaller. Many of the reported unpleasant experiences of synthetic cannabinoids relate to people putting amounts of synthetic material similar to a “normal” cannabis dose. At such levels people are more likely to experience unpleasant side effects.

Starter doses to assay strength and for those unfamiliar with synthetics should be no bigger than the head of a match. This should be mixed in with smoking material but NOT herbal cannabis. If being smoked in a pipe or bong, even smaller quantities may be indicated.

Potency may increase as people get to the bottom of the bag. If the psychoactive material is not firmly bonded to the smoking mixture, it can lead to “bottom of the bag” syndrome, where active ingredients can shake off and become concentrated in the bottom of the bag and can be unexpectedly potent.

METHODS OF USE: Most user reports indicate that synthetic cannabinoids are being smoked in the same way as spliffs – mixed in with tobacco and smoked. As very small quantities of synthetic material are required to achieve intoxication, smoking “straight spliffs” of smoking mixture alone without tobacco is not recommended, though users with a high tolerance will often be doing so.

Synthetic cannabinoids are also used in pipes and bongs. Given their relative potency and the small quantities needed to achieve intoxication, care is needed when using pipes or bongs to avoid unpleasant overdose experiences.

There have been reports of SCRA being snorted, swallowed and injected. As the latest products seem to have poor solubility in water, it is unclear how effective such routes would be.

EFFECTS: The effects of synthetic cannabinoids seem to be very variable and will depend on the user, their state of mind, the type of product used, dose and other substances involved.

For some people, the effect is akin to strong cannabis. This could include euphoria, altered perception, hilarity and a subsequent “stoned” feeling of relaxation and calm.

However, a significant number of users don’t report such symptoms and instead report anxiety, feelings of panic, disorientation and dysphoria – the opposite of sought-after euphoric feelings.

While these negative effects could happen to anyone, it seems to be more prevalent amongst people using high doses, or redosing, or people mixing their synthetics with alcohol or cannabis.

Unpleasant effects/risks:

As these compounds are so new, we know very little about what risks they may pose or what causes specific observed symptoms. Risks could stem from:

- the direct effects of the drug during use
- the mix of compounds used in a specific “blend”
- withdrawal symptoms after use
- toxic effects caused as the drug is metabolized in the body or from new unknown compounds formed as the drug is heated and burns or melts.

A number of users report distinctly unpleasant side-effects, above and beyond the panic or anxiety described above. These include:

Psychological:	Physical:
<ul style="list-style-type: none"> • Anxiety • Paranoia, panic, extreme fear reactions • Detachment, derealisation, depersonalisation • Auditory, visual, tactile hallucinations • Delusions, • Short lived or persistent psychosis • Fear-generated aggression • Loss of insight • Amnesia • Impulsive behaviour 	<ul style="list-style-type: none"> • Muscle tremors and spasms • Limb twitching • Paralysis (rigid and flaccid) • Convulsions • Elevated heart rate (160 BPM + for extended periods) • Nausea • Respiratory distress • Loss of basic functions • Kidney problems • Tolerance • High body temperature • sweating

As most of the synthetic cannabinoids are relatively new and untested, we do not yet know if they will cause long term problems. It is reasonable to think that they are likely at least to cause some of the same problems that strong cannabis does, including short term memory problems, lethargy, depression and demotivation.

We do not yet know if use amongst young people will increase the risk of psychotic-type illness, as heavy use of strong cannabis appears to. However, it would not be unreasonable to assume such a correlation will be a risk.

ACUTE EPISODES: “SPICE ATTACKS”

Workers in a number of settings, including hostels, prisons and emergency services describe in vivid terms the impact of high doses of SCRA and difficulty in managing people. Casualties may present:

- intensely panic
- unconscious
- convulsing or paralyzed
- delusional, hallucinating
- psychotic
- fearful or aggressive
- overheating.

There is no currently “reverser” or “antidote” for SCRA so management of casualties should be primarily symptomatic.

- If the patient is sufficiently lucid, explaining what is happening and reassuring them that they are safe.
- If the person is convulsing, the safe management of the convulsion should be the priority and the use of restraint avoided while the person is convulsing;

- In the event of overheating, measures may be required to reduce body temperature such as tepid water on the torso and exposure to moving cool air;
- If a person is very altered and presents a risk to themselves or others, they may need to be restrained if they are insufficiently lucid and can't be calmed via other methods;
- As the person exits the acute phase they are likely to be highly anxious, confused and lack memory of what has happened. Helping to explain what has happened and "contextualizing" their experience is essential.
- Medication may be required to manage acute symptoms such as anticonvulsants, anti-psychotics or to reduce heart rate.

“Chemical-induced PTSD?” A number of training participants (including former SRCA users) have highlighted recurring episodes of panic and anxiety after SCRA use has stopped. Thinking about how people experience intense panic during episodes of SCRA use, these flashbacks could be considered a form of PTSD. The person has effectively had the psychological experience of a traumatic event, without the actual trauma. The situation may be further complicated as many people experience amnesia post spice-induced episodes. This makes it harder to talk through and rationalize their experience. Helping people who experience such flashbacks to understand their experience through a model of PTSD may help them make sense of and manage these episodes.

Possible fatalities related to synthetic cannabinoids?

SCRAs have been implicated in a number of deaths, often where they have been used at high doses or in combination with other drugs. Deaths may have been the result of heart failure, convulsions, accidents when intoxicated or other causes.

REDUCING HARM: At present, without much more detailed information about specific synthetic cannabinoids it is not possible to suggest if any of the various substances on the market are more or less safe than others. Likewise, we can't speak with any certainty as to how safe or unsafe products may prove to be in the medium to long term

In lieu of more detailed information only the broadest of harm reduction messages can be offered, including the following:

- Potency is hugely variable: start with a very small dose (match-head size or less) and only escalate dose cautiously, giving time for previous doses to wear off;
- Some people report blends containing a mix of different chemicals can have more unpleasant side effects and should only be used with great caution;
- Be VERY cautious about using such compounds in bongs or pipes: it is harder to regulate intake and easy to take too much;
- Don't get into bouts of competitive use (e.g. in bucket bongs etc) as there is a high risk of overdosing;
- If sourcing pure powder synthetic cannabinoids, only use very small doses, calculated using scales and thoroughly mixed in to smoking material;
- Don't use in conjunction with other drugs, especially other forms of cannabis, alcohol or stimulants;
- There may be a risk of heart problems: you are best off avoiding these compounds if you have an existing heart problem or are using alongside stimulants;

- As synthetic cannabinoids may exacerbate anxiety and paranoia only use in an environment in which you feel safe, with people who you trust. Avoid using if prone to anxiety or have existing mental health problems;
- In the event of panic or anxiety, often treating as for panic attack will help resolve symptoms – sitting down, head down, regular breathing and reassurance. However more serious symptoms, including delusional behaviour or respiratory distress may require medical assistance;
- If you experience a sustained period of fast heart rate, or experience chest pains call an ambulance;
- Use can cause a comedown, development of tolerance, dependence and withdrawal symptoms. If using these compounds, don't use constantly and take breaks from use;
- Don't drive or operate machinery when using these compounds.

Some people report being accidentally or deliberately exposed to SCRA without intending to use them. This includes:

- Buying herbal cannabis which is mixed with SCRA
- Sharing spliffs, buying pre-rolled spliffs
- Smoking dog-ends
- Using e-cigs

To reduce risks of this sort of exposure, try to purchase from reliable sources, and inspect all cannabis for unusual smells or consistency. Exercise care with sharing spliffs and cigarettes.

TOLERANCE AND ADDICTION: With regular, frequent use tolerance can develop, leading to escalating doses. While naïve users may use a fraction of a gram per dose, heavy users may be getting through 10-15g or more per day.

Heavy users describe highly unpleasant withdrawal symptoms, lasting from a few days to a couple of weeks.

SCRA Withdrawal Symptoms:

- | | |
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| <ul style="list-style-type: none"> • Significant craving • Physical pain on stopping • Serious stomach cramps • nausea • Neural pain • Joint pain • headaches | <ul style="list-style-type: none"> • Sleeplessness, • Mood swings, intense irritability • Anxiety, panic attacks • Delusions and psychosis • Fluctuating body temperature • Sweating |
|--|--|

Treatment of Dependency:

There is little published literature on the management of SCRA dependency. Project Neptune is only half a page long. It advocates symptomatic treatments.

Symptomatic interventions have included use of Buscopan to manage stomach cramps but this was significantly misused in some prisons and so has been phased out in many settings.

Peppermint oil has reportedly been used to alleviate moderate gastro-intestinal problems.

Analgesia may be required – ideally non-opiate and, given risk of stomach problems from poor appetite and vomiting, aspirin may not be ideal.

Use of Nytol or similar to help with sleep in the short term may be beneficial.

A Shift to Opiates?

Anecdotally, people withdrawing from SCRA may describe their symptoms as being like opiate withdrawal. This has included ex-opiate users with experience of opiate withdrawal.

Faced with a lack of treatment services working effectively with SCRA addiction, some people have found relief via use of street-opiates, gravitating towards heroin, methadone or buprenorphine to manage withdrawal symptoms.

At present, with a reduction in access to SCRA it is essential that those currently dependent are able to access treatment before they switch to other patterns of drug use.

A tool to encourage a structured intervention for SCRA addiction can be found on the KFx website [here](#).

6. Management of the harms associated with long-term and frequent use

Very little evidence is available on the management of the harmful or dependent use of SCRA; it is suggested that clinicians adopt the evidence-based approaches used for other drugs – particularly natural cannabis.

There is no evidence to suggest that a particular approach is linked to successful outcomes for SCRA users.

Suggested psychological and social interventions include motivational approaches, relapse prevention and reintegration with non-using social networks.

No specific medications are indicated for SCRA harmful use or dependence and no substitute prescribing is currently available.

Symptomatic management of withdrawal symptoms may be indicated in some cases.

Whatever approaches are used, interventions should also address issues specific to SCRA and to particular populations who appear to be using them. Underlying drivers of use can include misuse of other substances, mental health and physical health comorbidity, issues associated with homelessness and deprivation, and involvement in the criminal justice system and incarceration.

There is no risk-free way to use SCRA, so it is important that people who continue using them have information to help them reduce adverse effects and harms.

OTHER INFORMATION:

For further information on synthetic cannabinoids the following sources will be useful:

Statutory/NHS/European

WEDINOS: <http://www.wedinos.org/index.html>

ACMD: Report on the Major Cannabinoid Agonists: 2009

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/119149/acmd-report-agonists.pdf

EMCDDA: Synthetic Cannabinoids and Spice Drug Profiles:

<http://www.emcdda.europa.eu/publications/drug-profiles/synthetic-cannabinoids>

EMCDDA: Understanding the Spice Phenomenon

Project Neptune: Harms of Synthetic Cannabinoid Receptor Agonists (SCRAs) and Their Management

<http://neptune-clinical-guidance.co.uk/wp-content/uploads/2016/07/Synthetic-Cannabinoid-Receptor-Agonists.pdf>

Discussion Groups:

Drugs Forum: <http://www.drugs-forum.com/index.php#>

Bluelight: <http://www.bluelight.ru>

Non-statutory information sources

Spice: the bird killer what prisoners think about the use of spice and other legal highs in prison:

User Voice:

<http://www.uservoice.org/wp-content/uploads/2016/05/User-Voice-Spice-The-Bird-Killer-Report-Low-Res.pdf>

Drugs Wheel: www.drugswheel.com

Drug Wise: <http://www.drugwise.org.uk/synthetic-cannabinoids/>

Isomer Designs: useful site with legal classifications:

<https://isomerdesign.com/Cdsa/scheduleUK.php?schedule=2§ion=25#>

Other Media:

BBC 3: Drugs Map of Britain: Getting off Mamba: <http://www.bbc.co.uk/programmes/p03nyf5k>

Vice: Spice Boys: http://www.vice.com/en_uk/tag/Spice%20Boys

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The participation of hundreds of training participants from a range of backgrounds have informed the contents of this document too.

Discussions and information shared on the DrugWatch discussion group were invaluable in preparation of this document.

ⁱ https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/380161/CannabinoidsReport.pdf

ⁱⁱ [https://ewsd.wiv-isp.be/Publications%20on%20new%20psychoactive%20substances/JWH-210/Huffman_SARfor%201-alkyl-3-\(1-naphthoyl\)indoles.pdf](https://ewsd.wiv-isp.be/Publications%20on%20new%20psychoactive%20substances/JWH-210/Huffman_SARfor%201-alkyl-3-(1-naphthoyl)indoles.pdf)

ⁱⁱⁱ <https://ewsd.wiv-isp.be/Publications%20on%20new%20psychoactive%20substances/JWH-251/1-Pentyl-3-phenylacetylindoles-a%20new%20class%20of%20cannabimimetic%20indoles.pdf>