Spice

Synthetic Cannabinoids (SCRAs)

New Psychoactive Substances
Briefing for professionals

Version 1.3 July 2017 1.3

Manchester Health & Care Commissioning
A partnership between
Manchester City Council
and NHS Manchester CCG

What is Spice?

Spice is a nickname for a herbal mixture containing one or more of a group of drugs called synthetic cannabinoids.

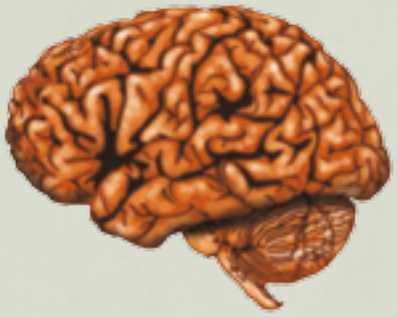
Spice was originally a brand name of a drug, sold as a 'legal high' along with other brand names like **Black Mamba, Annihilation, Exodus Damnation** and **Happy Joker**. They contained a non-psychoactive herbal smoking mixture that had been mixed with one or more of a group of drugs known as **Synthetic Cannabinoid Receptor Agonists** (to give them their full name) or **SCRA**s for short.

Spice (and Mamba) are now used as nicknames for any type of herbal mixture that has been coated with an SCRA. SCRAs can also appear as powders or liquids for use in e-cigarettes although in the UK SCRAs are now almost always smoked in a herbal form, however, SCRAs have also turned up as adulterants in a number of other drugs. In recent incidents in Oldham, pure crystals of SCRAs were sold as MDMA resulting in multiple hospital admissions.[1]

Since changes to the law in 2016,[2,3] Spice mixtures are now almost always sold in clear snap bags. On the street in Manchester Spice sells for approximately £5 for ½ and £10 for 1 gram bags.[4] Prices in prison are much higher.[5]

Spice was sold in branded packets but is now mainly sold in clear snap bags.

What are SCRAs?



SCRAs are made in a lab and stimulate the same areas of the brain as THC.

The cannabis plant contains a number of natural cannabinoids. **THC** (tetrahydrocannabinol) is the main one that gets you high.[5] **CBD** (cannabidiol) and **CBN** (cannabinol) have more relaxing and calming effects and moderate the effects of THC.[6,7,8]

Cannabinoids stimulate receptor sites called **CB1** and **CB2** (found in the brain and all over the body).[6,7,8] Stimulating these receptor sites leads to a wide range of effects on mood, thoughts, feelings and senses as well as a number of physical effects. SCRAs may bear no structural similarity to natural cannabinoids but, like THC, they also stimulate CB1 and CB2 receptors.[6,7,8] SCRAs may also have activity on the serotonin and dopamine systems.

SCRAs were designed by commercial research chemists in the 1980s, although they were never manufactured or clinically tested on humans.

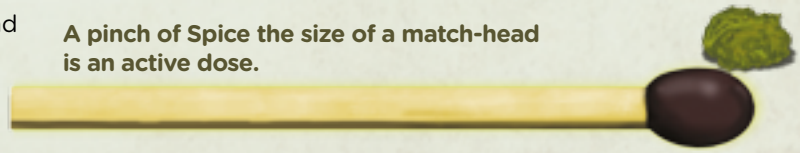
Why is Spice so potent?

SCRAs may have started out as legal cannabis substitutes, but the market changed and users wanted Spice products that were increasingly potent. Spice became an extremely potent product and quite unlike cannabis.

Cannabis only partially stimulates CB1 and CB2 receptors, whereas SCRAs can fully stimulate them. SCRAs have been described as 'Super stimulators' and can be up to 800 times more potent than cannabis.[9] SCRAs also may lack the calming effect of CBD/CBN found in cannabis.[9]

There are hundreds of different SCRAs, some much stronger and more toxic than others. The potency of a packet of Spice depends on which SCRAs are used and how much is added to the herbal mixture. Spice is potent even at very low doses: a pinch the size of a match-head is an active dose.[10]

A pinch of Spice the size of a match-head is an active dose.



Is Spice legal?

The original product sold under the brand name 'Spice' contained an SCRA called JWH-018. A range of SCRAs such as JWH-018 were made Class B under the **Misuse of Drugs Act in 2009**.

However, these were replaced in the shops within days by branded products containing a second generation of SCRAs that were not covered by the Misuse of Drugs Act such as AM-2201 (the drug in the original Black Mamba brand). These SCRAs were often more toxic and more potent than the ones they replaced.

The Misuse of Drugs Act was amended in 2013 so that AM-2201 and a range of other SCRAs were included. Hundreds of SCRAs were banned but within days these were again replaced with others not covered by the Misuse of Drugs Act.

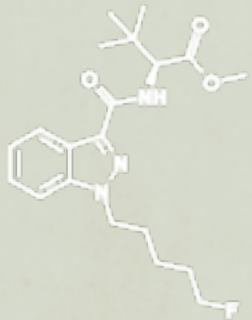
All SCRAs became illegal to sell, make, import and export in April 2016 under the **Psychoactive Substances Act,**[1] but were only illegal to possess in prison.

The Misuse of Drugs Act was amended again in December 2016,[3] so now most* of the known SCRAs and all those commonly found in Spice have become Class B drugs and are illegal to possess etc.

SCRAs are now mostly* Class B drugs.

* There are a number of SCRAs that although not currently in common use, are not controlled by the latest amendment to the Misuse of Drugs Act. These are MDMB-CHMCZCA, EG-018 (only seen as powder) and CUMYL-PeGACLONE.

Current Spice content



5F-ADB

SCRAs are mainly still made in China and imported as a powder into the UK, although there are unconfirmed reports of it being imported as a liquid via eastern Europe. SCRAs are then mixed (in a bath, cement mixer etc.) with a herbal smoking mixture in the UK and packaged into snap bags.

Since the advent of the Psychoactive Substances Act, little has been known about the SCRAs that are used in the Spice products sold in plain snap bags.[4] In March and April 2017 a number of Spice products were tested in Manchester[11] and the content varied in both the SCRA used and the ratio of plant material to SCRA. **In other words the potency and toxicity can vary between packets and may change from week to week.**

The SCRAs found in the test in March and April were all highly potent: **AMB-FUBINACA, AMB-CHMICA, 5F-AMB** and **5F-ADB**. [12,13,14,15] To make things even more confusing SCRAs are named in different ways. So for instance **5F-ADB** has a chemical long name of **N-[[1-(5-fluoropentyl)-1H-indazol-3-yl]carbonyl]-3-methyl-D-valine methyl ester.** It is known as **5F-ADB** for short but is also known as **5F-MDMB-PINACA.**[16]

Who is using Spice?

As stated Spice was originally sold as a 'legal high' designed to mimic the effects of cannabis and was used by a wide range of people, although nearly all of them had used illegal drugs before using Spice.[5]

As the product became more potent and developed a negative reputation it started to be associated with specific groups of people: prisoners, rough sleepers, psychiatric in-patients and young people often described as 'vulnerable'.[5] Drugs are not used in a vacuum and it is important to understand the particular issues these groups face when working with Spice users.[9]

"Whatever approaches are used, interventions should also address issues specific to SCRAs 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." [9]

"What we found was not that people were using Spice because they were bored but mainly as a coping mechanism and to self-medicate because the reasons why they are in prison in the first place have gone untreated."[17]

Drug screens & detection

Although Spice does have a smell when smoked, it is far less noticeable than cannabis and often is undetectable by smell alone when mixed with tobacco.

SCRAs cannot be detected by screening tests for THC. There are a number of specific drug screens for particular SCRAs but many new ones may not appear in simpler tests.[9]

The physical effects of Spice

Duration of Effects

The full effects are felt within seconds if smoked, before tailing off after 30 minutes to a more manageable state. Effects usually last 1-2 hours but can last much longer with some SCRAs. Spice is often smoked continuously throughout every waking hour (while supplies last).

Common physical effects

Tight chest, racing & irregular pulse, breathing difficulties, collapse, dizziness, numbness and vomiting are commonly reported physical effects of Spice.[9]

Physical problems

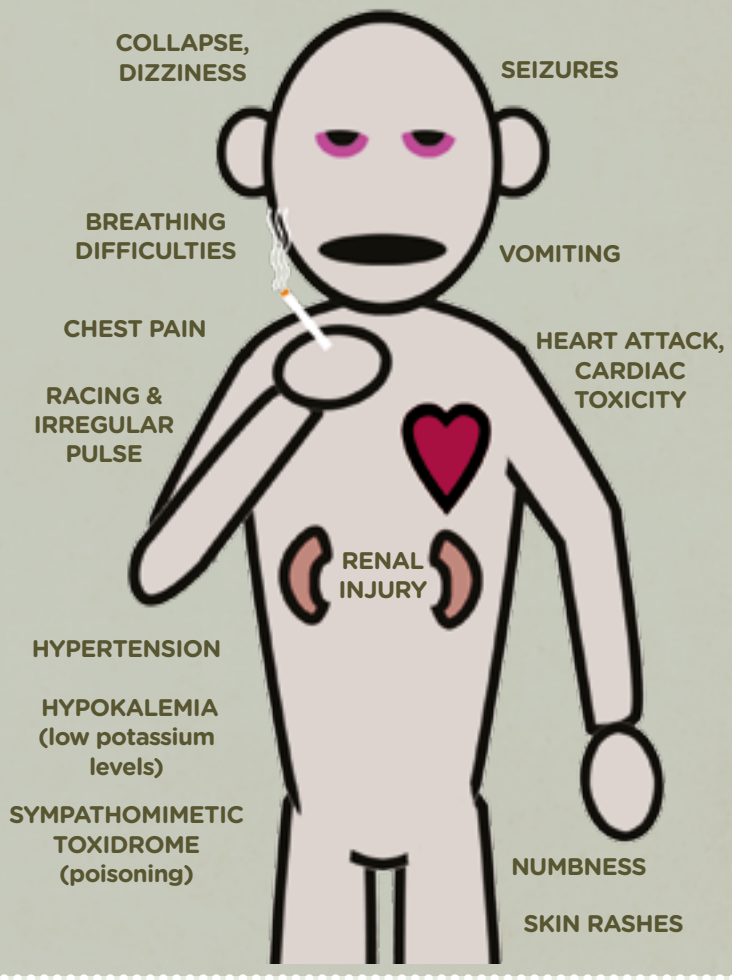
Seizures, cardiac toxicity, sympathomimetic toxidrome (poisoning), chest pain, heart attack, renal injury, hypertension, hypokalemia (low potassium levels), skin rash have been reported,[9] while other effects such as bleeding from the eyes and other orifices, teeth falling out are described by some long term users but have yet to be recognised in the literature.[5]

Emergency hospital admissions

There are no national figures for emergency admissions for Spice-related incidents, but could be estimated in the thousands per year. In one day in April 2017 in Manchester there were 58 ambulance call-outs reported that were related to Spice in the city centre, although some of these may have been related to the same incident.[18]

Death

Although ambulance call-outs and A&E admissions are common, deaths are relatively rare. 8 deaths associated with Spice were reported in England and Wales in 2015.[19]



The mental effects of Spice

For new users or in large doses, the mental effects of Spice can be overpowering. Effects are unlike cannabis and often described as, more akin to the effects of ketamine or solvents.

Spice can cause frightening visions or hallucinations. It can take you to what feels like a different reality, almost the same as this one, but a lot more scary. The mental effects together with the physical effects can cause panic.

"... the user will experience a true test of fate. Reality, perception, and consciousness will become severely altered to the point of one not knowing their own name, address, or that they are even a human being".[20]

Tolerance develops in a matter of days of regular use. The effects seem more exaggerated over time so a state often described as 'zombie-like' is commonly and constantly experienced by heavy Spice users. However, large doses or (as there does not appear to be cross tolerance) a different SCRA can bring on the more extreme state described even among experienced regular users.[9]

There are a wide range of mental effects described: anxiety, irritability and psychosis-like effects, inappropriate or uncontrolled laughter, anger, sadness, flat effect, depression and suicidal thoughts, excitability, agitation, combativeness, aggression, thought disorganisation, panic attacks, paranoid thinking, delusions, auditory and visual hallucinations, changes in perception, acute psychosis.[9]

Short-term memory and cognitive deficits, confusion, sedation and somnolence, thought blocking, nonsensical speech, amnesia and increased focus on internal unrest are also reported.[9]

Psychotic symptoms

"Psychotic symptoms appear to occur relatively frequently following SCRA consumption. More research is needed, but this may be linked to the high potency of the drugs and the fact that, unlike natural cannabis, SCRAs do not contain cannabidiol (CBD), a chemical which appears to possess antipsychotic properties."[9]

Dealing with Spice overdose

The number of Spice overdoses has placed a strain on already over-stretched emergency services. There are a number of simple guides to advise with when to dial 999.[21,22,23] However, these guides still require staff capable of taking blood pressure and accurately monitoring pulse rate and temperature.

The following visual guide is based on the DrugWatch Information Sheet,[24] Euro-DEN[21] and information from Project NEPTUNE.[9] It is aimed primarily at non medical professionals. In all drugs cases it is advisable to **treat the symptoms and not the drug**, as more than one drug may have been used and people may not have taken the drug(s) they think they have.

Spice Intoxication: people who have used Spice may act in a disturbing way, be unsteady and appear 'zombie-like' with pale skin and pink eyes. They will be confused, unable to communicate properly and may repeat actions, as short term memory is severely affected. However in the vast majority of cases people will not require emergency treatment.[9]
If in doubt call an ambulance.

Hallucinations, blabbering, incoherent, zombie-like behaviour, panic attacks, repetitive nonsensical actions are common when using Spice. Take them somewhere quiet where they feel safe (a low stimulus environment). Make eye contact, build trust. **Calm and reassure them.** If they become panicky and you notice them breathing very fast, get them to control their breathing by slowing it down or breathing into a paper bag.

Vomiting/feeling unwell: vomiting is nature's way of saying you've had too much. If somebody is unwell, don't give them anything to eat and only let them drink water. If after vomiting they want to sleep, let them but keep your eye on them. Make sure they are lying on their side **(the recovery position)**

Temperature over 38.5°C, not settling after about 5 minutes of rest or, if no thermometer is available, if very flushed and feels very hot. **Call an ambulance.**
If they are overheating: cool them down by removing outer clothing, fan them, use a wet cloth on their skin, take them outside or somewhere cool. If they are conscious allow them to sip water or a non alcoholic drink.

Serotonin syndrome: some SCRA compounds may increase the risk of serotonin syndrome.[9]

The main symptoms: rigid, jerky, twitchy unusual movements, often involving the legs shaking, fully dilated pupils, overheating, shivering, racing heart, agitation and confusion.

Severe chest pains: sit them down in a calm environment and reassure them. **Call an ambulance.**

Heart rate over 140 beats per minute, not settling within 5 minutes. **Call an ambulance.**

Seizures (convulsion similar to an epileptic fit). Make sure the area is safe and there is nothing they could hurt themselves on. **Call an ambulance.** Inform paramedics if the fit stops and starts, if it doesn't stop within a couple of minutes or if the person turns blue. **It is important not to hold people down because of the risk of rhabdomyolysis.**

Breathing difficulties, such as fast breathing rate, not settling within 5 minutes. If there is no breathing or it is abnormal (e.g. death rattle, agonal breath) then CPR should be attempted.
Call an ambulance.

Unconsciousness: it can be risky to startle or frighten people intoxicated on Spice as this can lead to heart failure. If they can't be woken by gentle shaking and calling, or you notice a blueness of the skin, including lips or fingernails (or greyish with paler lips for darker complexions), make sure they are lying on their side so they don't choke on vomit and **call an ambulance.**

Other concerns: e.g. severe vomiting, frothing at mouth, severe headache, significant agitation or aggression, not settling within 15 minutes. **Call an ambulance.**

SCRA interaction with medicines

Little is known about the risks of using SCRAs with other drugs, alcohol or medicines, let alone specific risks with different SCRAs. Any drug combinations should be considered potentially dangerous. Some SCRAs may be associated with activation of serotonin receptors. Due to the lack of clear information, decisions about continuity of prescribed medicines should be made on a case-by-case basis.[25]

It is advised that essential medication, such as insulin or warfarin is maintained but monitored. Given the association between SCRA use and convulsions, it is important to maintain prescribing of antiepileptic drugs. [25]

Interacting medicine (list not exhaustive)	Potential effect
Antifungals: itraconazole, ketoconazole, fluconazole **Macrolide antibiotics:** clarithromycin, telithromycin, erythromycin **Anti-HIV drugs:** indinavir, nelfinavir, ritonavir, saquinavir **Antipsychotics:** clozapine, quetiapine	These medicines inhibit the liver enzyme CYP3A4. This leads to an increase in plasma level of SCRA and decreased rate of clearance which potentiates its toxicity. Concomitant use may cause brain, kidney, liver or heart injury.

Chart based on information from PHE[25]

Tolerance, dependence & withdrawal

Dependence

Psychological dependence can occur with any substance, but physical dependence and a recognised withdrawal from SCRAs are beginning to be recognised in literature. [9] Services commonly report that the most noticeable effect of SCRA dependence is a change in behaviour, with people becoming withdrawn and aggressive often resorting to crime to pay for SCRAs.[5]

Tolerance

Tolerance to SCRAs is rapid; it has been reported that within a week of commencing use that 6 grams a day or more is used.[5] It is often stated that Spice is used in every waking moment and often waking from disturbed sleep to smoke in the middle of the night.[5] It is commonly stated that within days of first use the initial extreme effects (falling over, altered reality) are moderated into a state described as somewhere between heavy cannabis intoxication and a heroin 'gouch'.[5] However, it is also reported that there is no 'cross-tolerance' between different SCRAs and when the specific SCRA in a batch of Spice changes, the full 'extreme' effects are felt again.[5]

Withdrawal

Anecdotally, physical withdrawal is widely reported (and in fact is the norm) among people describing experiences of SCRA addiction. [5] The withdrawal profile is similar but more intrusive and intense than seen with 'skunk' withdrawal. Diaphoresis (extreme sweating) and insomnia/sleep disturbance are the most common and noticeable withdrawal symptoms,[5] with some often waking with bed sheets soaked. Stomach cramps are reported anecdotally and some describe mental disturbances that can continue for months after use has ceased.[5]

Withdrawal symptoms including; headaches, anxiety, coughing, impatience, difficulty concentrating, anger/irritability, restlessness, nausea, depression, craving, tremor and hypertension are recognised in the literature.[9]

Drug treatment

There is drug no substitute therapy known for Spice; drug treatment involves prescribing to alleviate withdrawal symptoms.[9]

Treatment for withdrawal

Short term benzodiazepines (such as diazepam) are used to assist sleep, manage anxiety, panic and agitation. Treatment with intravenous benzodiazepines has been reported for the management of seizures and in some cases of SCRA-related psychosis.[9]

There are some reports describing antipsychotic medication being indicated for some patients, especially those who present with agitation or aggression, when the patient has a history of psychotic disorders, and when the psychotic symptoms do not remit with supportive care. There are also a small number of reports that describe antidepressants being administered in cases where there is concurrent depression.[9]

Psychosocial treatment

Very little evidence is available on the management of the harmful or dependent use of SCRAs; 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.[9]

The FRAMES model[26] (feedback, responsibility, advice, menu of options, empathy, self-efficacy), initially developed as a brief intervention for risky or harmful alcohol consumption can be an effective means of engagement and retaining people in treatment. It can be used in a formal or intuitive way, and it is reported to be effective in the context of managing SCRA use in prisons.[25]

Anecdotally, users often try to withdraw by reducing SCRA use and self medicate by switching back to cannabis. However the effects of even potent 'skunk' often seem weak compared to SCRAs, so it may be several weeks after ceasing SCRA use before potent cannabis is an effective substitute.[5]

Harm reduction

Spice is a highly addictive, highly toxic drug that can and has killed people.
The following advice is designed to reduce some of the risks for those already using Spice,
but there is no safe way to use Spice. Spice users should be advised to seek help.

There is no safe way to use Spice
It is not the same as cannabis. Spice is more potent, more unpredictable and more dangerous.

It is illegal to possess (most) Spice
Most synthetic cannabinoids, the chemicals in Spice, are illegal to possess, are now are covered by the Misuse of Drugs Act as Class B drugs.

Spice varies from batch to batch
Different packets can produce different effects.

Sit down before you use
In case you fall over.

Start with a very small dose
Use a match-head size (or less) test dose with every new packet. Potency is hugely variable.

Wait before the effects have worn off before smoking more

Spice should not be smoked neat
Always smoke with a 'mixer' (e.g. tobacco or dried herbs).

Use thin cigarette papers
If smoking in a joint use thinnest papers and avoid using printed card for a roach to avoid inhaling additional fumes.

Avoid using Spice with other drugs
Avoid using with cannabis, alcohol or stimulants, this may raise the risk of heart problems.

Avoid mixing Spice with medicines and alcohol.

Be cautious with pipes
Be cautious about dosing in pipes or vaporisers: it is harder to regulate intake and easy to take too much. If smoking in a pipe, use small glass or steel pipes which give off less fumes than wood or plastic pipes.

Be VERY cautious about using in bongs
It is harder to regulate intake and easy to take too much. Water pipes also causes you to inhale more deeply which can cause more lung damage.

Don't get competitive
There is a high risk of overdosing if you get into bouts of competitive use (e.g. in bucket bongs etc.).

Beware the bottom of the bag
Be careful with dosing the crystalline powder material in the bottom of the bag; use a smaller dose, as this is generally stronger than the plant material which is coated with the SCRA.

Careful with powder
If sourcing pure powder SCRAs only use very small doses, calculated using scales and thoroughly mixed into smoking material.

Spice is very addictive
Regular use of Spice can lead to dependence (addiction) and withdrawal.

Spice is dangerous
Spice can cause severe harms. If you experience a sustained period of fast heart rate or chest pains, call an ambulance.

Spice can make you anxious
Spice may exacerbate anxiety and paranoia. Only use in an environment in which you feel safe, with people you trust.

Spice can make mental health problems worse
If you suffer from anxiety or mental health problems, avoid using Spice.

Do not drive or operate machinery under the influence of Spice.

Harm reduction advice for SCRA users should take into account underlying issues that groups such as prisoners or rough sleepers face.[9]
This harm reduction advice is based on[10,24,27].

Help available for Spice users

There are various treatments for Spice users including medically assisted withdrawal.

Achieve Salford Recovery Services
Adult teams:
The Orchard
2 Langley Road South
Salford, M6 6GU

Telephone 0161 358 1530

Achieve Salford Recovery Services
Young People team:
Beacon Centre
1 London Street
Salford, M6 6QT

Telephone 0161 358 1858

Spice: Synthetic Cannabinoids (SCRAs)
No 1 of an occasional series of briefings on New Psychoactive Substances for professionals in Manchester
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