

INTRODUCTION

- **Synthetic cannabinoids (SCs)** are a heterogeneous group of substances created in the 1960s
- SCs emerged as potential therapeutic targets in the context of endocannabinoid system research
- Over the last decade, SCs have become increasingly **popular as a substance of abuse** and sold under the names of **"Spice"** or **"K2"**
- Growing evidence suggests that, compared to natural cannabis, SCs are **associated with**:
 - More **rapid** development of **dependence**
 - **Increased psychiatric symptoms/illnesses**
 - **Serious physical adverse effects**

OBJECTIVES AND METHODS

This work provides an overview of the mechanism of action of SCs, as well as the potential physical and psychiatric consequences of its chronic use. A non-systematic review of the literature was performed using Pubmed database.

RESULTS

Synthetic Cannabinoids (SCs) are classified based on the chemical structures of the molecules.

- The most frequently investigated SCs are aminoalkylindole WIN55,212-2, the cyclohexylphenol CP55,940, and HU-210

SCs Mechanism of action

- **Delta-9-tetrahydrocannabinol (THC)** is the primary psychoactive component in the cannabis plant
- THC effects occur via the **endocannabinoid system**, which comprises the **cannabinoid receptors type 1 and 2 (CB1R and CB2R)**
- Unlike THC, **SCs** are **high-potency, high-efficacy, full agonists** at the brain's cannabinoid receptors, which implies greater harmful effects, and a longer duration of action
- Although most SCs are known to be potent CB1R agonists, knowledge of the exact mechanisms of action are limited
- Spice products (SP) comprise several SCs, and their **potency at CB1R and CB2R differ**, which may lead to different signalling mechanisms
 - ✓ SCs with a higher affinity for either CB1R or CB2R were shown to elicit adverse neurobehavioral effects
 - ✓ The **majority** of SCs found in SP were shown to have **higher affinity for CB1R** than CB2R
 - ✓ **Some** designer drugs found in SP **act through non-CB1R and CB2R targets**

- Chronic SCs users may have structural central nervous system abnormalities such as overall **reduced grey matter volume**

Psychiatric Consequences

Studies have found important impact of SCs in the development of psychiatric symptoms/disorders such as:

- Psychosis
- Acute anxiety and panic
- Mood swings (irritability, depression, suicidal ideation)
- Memory and attention deficits

Daily use of high-potency cannabis such as SC's has been linked to earlier onset of psychosis in cannabis users

Physical Consequences

SCs use may result in:

- Tachycardia, hyperventilation, hypertension, diaphoresis, chest pain, palpitations
- Agitation, myalgia, tremor
- Nausea, vomiting, diarrhea, headache

Severe adverse events may occur:

- Stroke
- Seizures
- Myocardial infarction
- Death

CONCLUSIONS

Growing evidence shows the risks and potential harms of SCs use, with solid evidence linking these substances to psychotic illnesses such as schizophrenia. It is important for clinicians to be aware of these risks for an improved management of adverse events and a better understanding of cannabinoid pharmacology in humans.

REFERENCES

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