Saccharomyces cerevisiae as a toxicological model to study synthetic cannabinoids and its pyrolysis products

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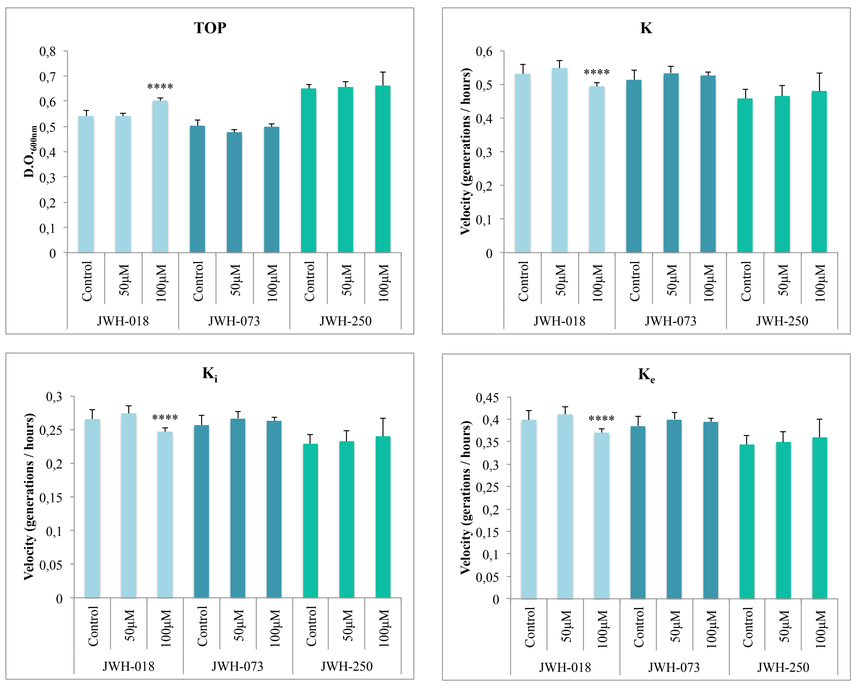
INTRODUCTION

Synthetic cannabinoids are among the major psychoactive drugs widespread as safe and legal alternatives to cannabis. They are commercially available as herbal incense products intended for smoke[1]. This has led most of developed countries to concentrate efforts in order to ban the so called “legal highs”. Despite of their increasing use, there is still a lack of information on both synthetic and natural ingredients, pharmacokinetic properties and toxic effects. In fact some of the substances seem to have stronger toxicological effects when compared to their legal counterpart[2-4]. Toxicological assays are paramount to know how harmful these new substances are, helping increase public awareness since several hospitalization cases have been reported due to consumption[2-4].

To tackle the new challenges posed by novel drugs worldwide, we developed an approach using *Saccharomyces cerevisiae* as a model to investigate the toxicity of pyrolysis products of synthetic cannabinoids. *S. cerevisiae*

RESULTS



TOP: final biomass; K: velocity in the initial of exponential phase; K_e: velocity in the middle of exponential phase; K_i: velocity in the end of exponential phase

Fig. 1 – **Growth kinetics with synthetic cannabinoids.** The cells grew at 30ºC in minimal medium (0,67% YNB; 2% Glucose; Amino acids) in the presence of synthetic cannabinoids in DMSO and just in the presence of DMSO (control culture). These results suggest that the yeast growth is just affected by JWH-018 (****p<0,1).

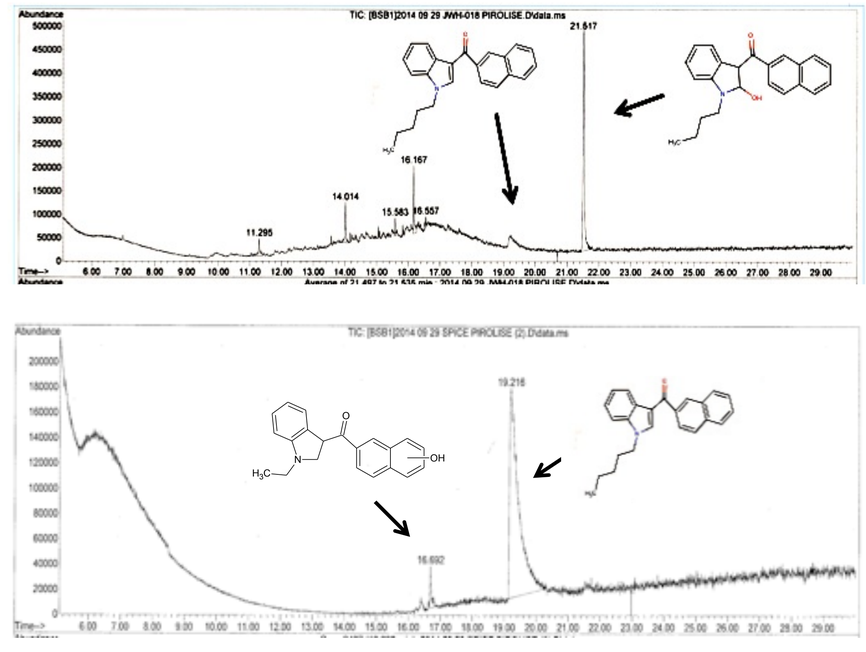


Fig. 3 – **Confirmation the efficience of pyrolysys system.** JWH-018 and SPICE were burned and the results were analysed by GC-MS. These results shown that were produced 2 pyrolysis products of JWH-018

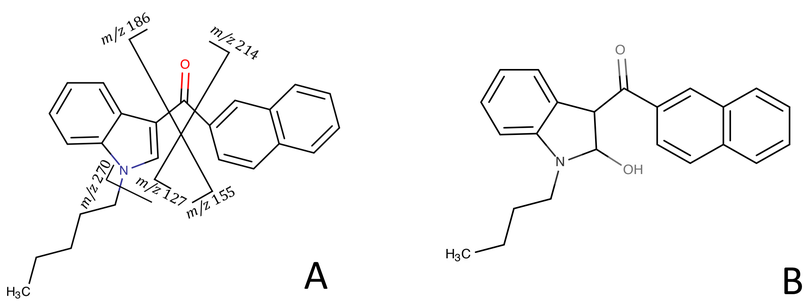


Fig. 2 **Typical fragmentation and oxidation of pyrolytic products.** The pyrolytic system consists of a pipe connected to two traps under vacuum, one with MilliQ water, to retain hydrophilic products, and the second contains dichloromethane in order to capture hydrophobic products. Above are the two main types of modification during pyrolysis: Fragmentation and hydroxylation. (A) JWH-018 with types of fragmentation; (B) Pyrolytic product of JWH-018 with hydroxylation and a fragmentation in alkyl group.

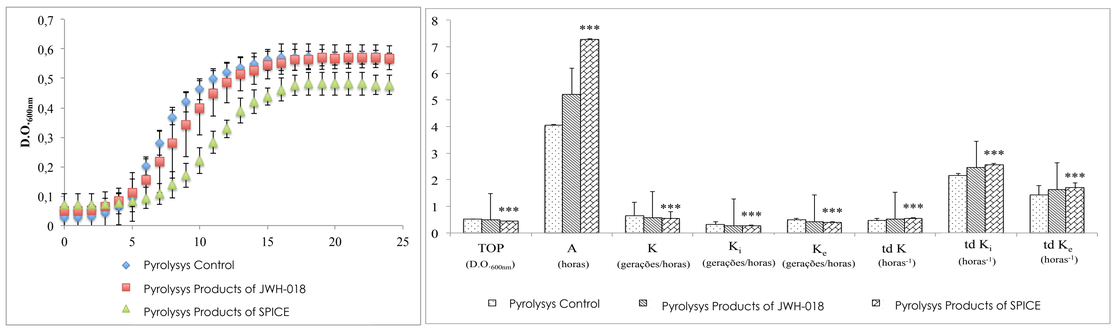


Fig. 4 – **Growth kinetics with pyrolysis products.** The cells grew at 30ºC in minimal medium (0,67% YNB; 2% Glucose; Amino acids) in the presence of pyrolysis products of synthetic cannabinoids in DMSO and just in the presence of pyrolysys control (control culture). These results suggest that the yeast growth is affected by pyrolysis products of JWH-018 but the cellular growth has a major increase in the presence of pyrolysis products of SPICE (***p<0,05)

CONCLUSIONS

Our results points yeast as a contradictory model when studying the toxicological impact of smoked substances and pyrolysis products. While synthetic cannabinoids seems not to produce much effect on yeast, pyrolysis products has a clear effect. We are now studying the effect of this substances in the cellular proteome.

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