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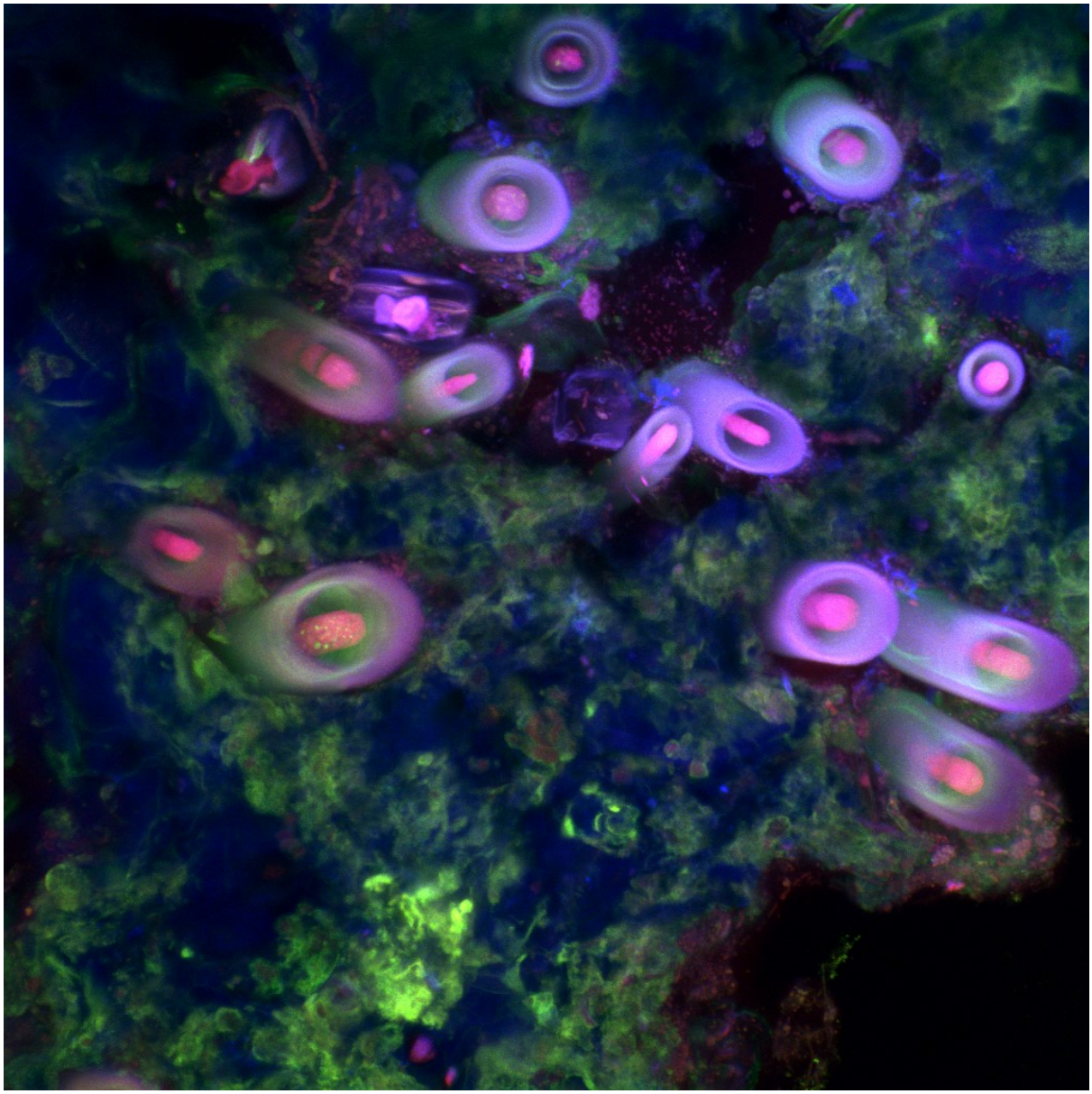

SAIB-SAMIGE Joint Meeting 2020 – *Online*

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LVI Annual Meeting
Argentine Society for Biochemistry and Molecular Biology
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Joint Meeting 2020

MI-P52-258
A NEW CHROMENE FLAVANONE FROM *Dalea boliviana* BRITTON (FABACEAE) AGAINST *Candida tropicalis* BIOFILMS

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Currently, a wide variety of natural products are used for medicinal purposes, both to prevent and treat health problems, as well as in the research and development of new drugs. Previous studies on the species *Dalea elegans* Gillies ex Hook. et Arn, led to the isolation and elucidation of a prenylated flavonoid: 2',4'-dihydroxy-5'-(1''',1'''-dimethylallyl)-8 prenylpinocembrin (8PP). This compound exhibited antimicrobial activity against bacterial and fungal strains and was also reported with activity against *Candida albicans* mature biofilms. This species is the most frequently isolated from candidiasis, however, the incidence of fungal infections produced by *C.* non-albicans has increased in recent years in Latin America. Antifungal treatment can be difficult, often associated with the ability to form a biofilm, with high resistance to antifungal agents. This work aimed to perform the chemical study and evaluations of the antibiofilm activity of the species *D. boliviana* Britton (Fabaceae) as a potential source of new structures for the investigation of antifungal drugs. The chemical study of *D. boliviana* was performed by obtaining the hexane extract from its roots. This extract was purified by column chromatography and thin-laye chromatography. A solid, amorphous, and orange-colored compound (**N3**) was isolated and purified. N3 structure was determined by spectroscopic methodologies (NMR H^1 and C^{13} in one and two dimensions) and UV-Vis spectrophotometry. **N3** activity was evaluated *in vitro* on mature biofilms of *C. tropicalis* (NCPF 1111). The mature biofilm was treated with **N3** dissolved in dimethyl sulfoxide (2% DMSO), at a final concentration of 25 µg/mL, with Amphotericin B (AmB) at 100 µg/mL, and with the combination of both. The results were reported as relative percentages of inhibition with respect to the control (mature biofilms without treatment). As a result of the analysis of the spectral data, the new structure named 5,2'-dihydroxy-6'',6''-dimethylchromeno-(7,8:2'',3'')-flavanone (**N3**), is postulated. It is a chromeno flavanone reported for the first time in the species *D. boliviana*. Compound **N3** by itself reduced 54 ± 4% of the mature biofilm of *C. tropicalis*, while Amb reduced 86 ± 2%. For the combination of both compounds, the inhibition resulted in 98 ± 3%. In conclusion, this work presents a new compound obtained from the Argentine native flora showing activity against a highly resistant structure such as the mature biofilm of *C. tropicalis*. Furthermore, when the compound **N3** was combined with AmB, the total eradication of the biofilm was obtained. Since *Candida* biofilms have marked resistance to antifungals for clinical use, it is important to obtain new active compounds against this form of growth, so it would merit the continuity of this research, especially in the search for synergistic combinations and studies on the mechanism of action.

MI-P53-259
ELUCIDATION OF ACETIL-COA METABOLISM IN *Streptomyces coelicolor* THROUGH STABLE ISOTOPE-ASSISTED METABOLOMICS

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The genus *Streptomyces* plays key roles in soil ecology based on their ability to scavenge nutrients and recycling deth insect and plants by hydrolysing polysaccharides like cellulose, chitin, xylan, and agar. However, the most interesting characteristics of *Streptomyces* spp. rely on their ability to produce bioactive secondary metabolites –such as antifungals, antivirals, antitumorals, and antibiotics– and their capability of accumulate triacylglycerols (TAGs). TAGs and some secondary metabolites (polyketides) are produced mainly from a key central precursor: acetyl-CoA. This acetyl-CoA participates in other important pathways, like Krebs cycle, and it is a precursor of several macromolecules. Nevertheless, how these bacteria assimilate acetyl-CoA precursor to produce building blocks and the influence of this assimilation on the production of secondary metabolites and TAGs in actinobacteria is poorly understood. With the purpose of understanding the metabolism of acetyl-CoA and its role in TAGs and secondary metabolite biosynthesis, a study about the assimilation of acetyl-CoA in *Streptomyces coelicolor* was started. Genomic analysis showed that in *S. coelicolor* there are two putative pathways for acetyl-CoA assimilation, the glyoxylate cycle (*sco0982-0983*) and the ethylmalonyl-CoA pathway (*sco6469-6473*). By constructing single (*Δsco0982* or *sco6473::Tn5066* (Hyg^R)) and double mutants deficient in these pathways (*Δsco0982* and *sco6473::Tn5066* (Hyg^R)), it was found that *S. coelicolor* still grow on minimal medium with acetate as the only carbon source, which suggests that there is a novel unknown pathway for acetyl-CoA assimilation. With the aim of identifying the acetyl-CoA metabolic intermediates in both, wild type and the double mutant strains of *S. coelicolor,* a stable isotope-assisted metabolomics with C13-Acetate was carried out. For this purpose, both strains were grown until exponential phase in minimal medium with acetate as only carbon source and then labelled acetate was added. The incorporation of the labelling was allowed for 0, 5, 10, 30 and 60 min. After this, the cytoplasmic metabolites were extracted, and the samples were run in a Q-exactive mass spectrometer. Metabolic analysis showed no differences between both strains, suggesting that the double mutant strain uses an acetyl-CoA assimilation pathway similar to the parental strain. Analysis of the sample also showed that central metabolites like glutamate, succinate, citrate, among others were labelled at early times. These are consistent with the intermediaries of some acetyl-CoA assimilation pathways of archaea, like the methylaspartate cycle. Currently, genetic studies are being performed with the aim to identify homologous genes of this pathway that could be involved in acetyl-CoA metabolism in *S. coelicolor*.