The effect of β-Carbolines on gut microflora in relation to psychedelic drug absorbance

β-Carbolines are a group of indole alkaloids that can be found in 23 different angiosperm species. β-Carbolines have been a topic of interest due to their pharmacological functions, ability to intercalate with DNA and the vast neuropharmacological effects β-Carbolines can have on an organism. Indigenous people from the Amazon Basin have utilised β-Carbolines for thousands of years in the form of Ayahuasca. Ayahuasca is a traditional Amazonian brew containing β-Carbolines (harmine and harmaline) from a vine (*Banisteriopsis caapi*) and N,N-dimethyltryptamine from the leaves of a bush (*Psychotria viridis*). N,N-dimethyltryptamine (DMT) is a highly psychoactive compound which is traditionally used for evoking entheogenic experiences. When orally ingested on its own, DMT is rapidly metabolized in the gut by enzymes called Monoamine oxidase therefore preventing the effects of the compound. DMT is combined with harmine and harmaline in Ayahuasca as these β-Carbolines interact with the enzymes and act as monoamine oxidase inhibitors (MAOIs), allowing the DMT to induce an altered state of consciousness for several hours.

There appears to be limited information about particular intestinal microflora that may assist in the production of beta-carbolines. Although there appears to be comprehensive research into the mechanisms of gut microflora in relation to drug absorption, there is a finite amount of studies that have been conducted to investigate the absorption of psychedelic substances.

The aim of this research report is to understand what effects the β-Carbolines, harmine and harmaline, have on certain gut microflora and whether consuming an excess amount of these harmala alkaloids affects the growth of E.Coli as a representative species present in gut microflora. The source of harmine and harmaline is passionflower tea (*Passiflora incarnata*).

Through analysing bacterial growth and interactions between passionflower and E.coli within the small environment of an agar plate, it is clear that β-Carbolines play a role in microflora growth. Although more research is needed as there are a plethora of colonial microflora that reside in the human gastrointestinal microbiome that directly affect health on different levels, mental and physical, therefore it is vital to understand β-Carboline interactions and effects on gut health.

Literature Review:

Studies recently into the microflora capacity in direct relation to the catalytic capability of psychedelic absorbance is limited. Other scientific studies (J. Mabit, 2001)(Ly et al., 2018) have suggested that the microdosing of psychedelics has a positive influence on anti-addictive therapy. This review seeks to identify avenues of research into common dietary beta-carbolines present in the Western diet and its effect on psychedelic drug absorbance.

Discussion:

When analyzing the results, there appears to be no inhibited E.coli growth and instead an interaction between harmala alkaloids and the E.coli colonies is evident. These interactions can be described as competitive and promotional. When comparing plate 1B (Fig. 1) and the E.coli control (Fig. 3) it is clear that the passionflower has accelerated the growth of E.coli through microbial competition. Microbes often compete for nutrients when occupying a common environment (Fredrickson and Stephanopoulos, 1981). During this competition for resources, some microbes will release toxic chemicals or enzymes to inhibit the growth of other species (Fredrickson and Stephanopoulos, 1981). Although plate 1B (Fig. 3) displays competition for resources, there is no evidence of inhibition which indicates co-existence between the β-Carbolines and E.coli colonies. Co-existence is seen throughout the agar plates, this could be linked to E.coli being a heterotrophic organism, meaning nutrition is obtained through an external source (Gleizer et al., 2019). When taking this into consideration, it could be proposed that co-existence is occurring because the passionflower is providing a sustainable amount of nutrients in order for E.coli colonies to flourish. Figures 2,6,7,8 and 9 all show microbial interaction with no inhibited growth. Plate 7A (Fig. 7) is a great example of microbial interaction as it displays the swimming flagella-driven motility of E.coli (Gómez-Gómez, Manfredi, Alonso and Blázquez, 2007). This swimming motility indicates the attempt of E.coli to reach more resources in order to thrive (Gómez-Gómez, Manfredi, Alonso and Blázquez, 2007). When analysing the results there is always a clear promotion of E.coli growth but Plate 8B (Fig. 9) displays a burst of colony expansion specifically around the paper disc that was soaked in solution 9. This suggests that an increase in β-Carboline concentration leads to higher microbial growth. The table (2) seen above demonstrates that the average microbial growth of group B (92.3%) is slightly higher than group A (89%-90.4%). This indicates that the concentration of passionflower tea as a source of β-Carbolines does not inhibit microbial growth but in fact promotes growth.

The experimental control (Fig. 4) displayed no signs of cross contamination confirming that the results gained from the experiment were not compromised. The passionflower tea (Fig. 5) and E.coli control (Fig. 3) provided a reference and a source of identification when analysing

the agar plates and the interactions between colonies.

Percentage grid counts were used to calculate the amount of bacterial coverage across the agar plates. Although this method has provided an appropriate approximation of bacterial coverage, there is a margin of error that must be considered and a more accurate method of data analyses could be used. For example, with more time and resources the number of colony forming units per milliliter of agar could be calculated therefore resulting in a more accurate reading of the microbial growth that has occurred. This can be regarded as a limitation within the experiment. Another limitation is determining whether harmaline and harmine are the chemicals promoting microbial growth and not another chemical from the passionflower tea. To resolve this, the experiment should be repeated using different sources of β-Carbolines such as *Banisteriopsis caapi* which is used in ayahuasca tea or the Syrian rue which contains 2% to 4% of β-Carbolines (Cornell University Department of Animal Science, 2018). Higher β-Carboline content could provide more accurate results. The accuracy of this experiment could also be increased by finding a way to extract and isolate harmine and harmaline to investigate the direct effects on gut microflora without interference of other bacteria.

Although the results heavily support the hypothesis of the link between microbial growth promotion of E.coli and the concentration of β-Carbolines, the human gastrointestinal microbiota possesses an estimated 300 to 500 different bacterial species (Quigley, 2013). This means further research into the effect harmine and harmaline have on gut microflora is needed in order to build a broader picture of the potential benefits and dangers of these substances when paired with certain psychedelics like DMT in relation to treating illnesses such as addiction.

Conclusion:

Through analysing the data collected, there is an apparent correlation between concentration levels of β-Carbolines (harmine and harmaline) and the amount of colonial growth seen within the agar plates. The results concur with the scientific hypothesis as well as answers the scientific questions that were posed earlier in the report. This suggests that not only do harmaline and harmine act as enzyme inhibitors that allow for psychedelics to be readily absorbed within the body leading to intercortical

reframing potentially resulting in the disintegration of addictive behaviours or other mental illnesses but also promotes gut health and microflora production. Although the results are supportive of the hypothesis, it is vital to investigate the effects of β-Carbolines on the growth of other bacterial species that belong in the human gastrointestinal microbiota, as they all play a pivotal role in the holistic health of human beings. Addiction is becoming an epidemic in westernised societies. The use of psychedelic compounds to create alternate neural pathways and increase prefrontal cortex plasticity (Ly et al., 2018) provides individuals with the tools to break away from addictive behaviours. Through psychedelic-assisted psychotherapy the toughest of mental illnesses could be resolved and better understood, providing people with the ability to live a better life.

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