Metformin Inhibits Bacterial Glycerol Metabolism: Implications for Medicinal Effect

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Metformin is the most commonly prescribed antidiabetic drug in the world, being a valuable drug for not only treating diabetes, but also metabolic syndrome, pre-diabetes, obesity, and perhaps even cancer. Despite metformin widespread use, patients that fail to respond to metformin therapy reaches as high as 35%. An unexplored contributor to variability in metformin efficacy is the human gut microbiome. Insight may be gained by seeing how the human pathways are affected by metformin by identifying bacterial targets. The ultimate goal of this project was to determine the effect of metformin on intestinal bacterial catabolism of glycerol as a carbon source. It was hypothesized that metformin influences the mammalian microbiome composition by inhibiting aerobic catabolism of glycerol by bacteria. A mixed culture assay was conducted to examine metformin's effect on bacterial growth on specific carbon sources. The results showed that metformin inhibits E. cloacae and P. aeruginosa growth on glycerol. Both of these bacteria oxidatively catabolize glycerol and neither strain can ferment glycerol. Therefore, the results suggest that oxidative catabolism of glycerol is inhibited. Furthermore, metformin does not inhibit the growth of E. aerogenes or K. pneumonia, both of which have multiple metabolic pathways for catabolism of metformin including fermentative pathways. The results suggest that the presence of fermentation pathways for glycerol catabolism provide resistance to metformin inhibition of growth on glycerol. It is concluded that metformin alters the metabolism of the gut bacteria which can affect short chain fatty acid production and offer further knowledge on medicinal usage. Further experimentation is required.

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