## PP-D-15

### EFFECT OF CITRAL ON NONALCOHOLIC STEATOHEPATITIS (NASH) VIA AMPK-MEDIATED AUTOPHAGY AND INFLAMMASOME PATHWAY IN TYPE 2 DIABETIC MICE

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#### OBJECTIVES
Nonalcoholic steatohepatitis (NASH) is the progressive form of non-alcoholic fatty liver disease (NAFLD), associated with lipotoxicity-induced autophagy defects and significantly increased inflammasome expression. Citral, a terpenoid and the main constituent of Lemongrass, is reported to have multiple biological activities. This study aimed to investigate the effect of citral on mechanisms underlying the relationship between the autophagy Inflammatory and lipid metabolism-related gene deregulation associated with NASH using an in vivo model of type 2 diabetes.

#### METHODOLOGY
Thirty male BALB/c mice were randomly divided into three groups: control (n = 10), model (n = 10), and treatment (citral) group (n = 10). Mouse models of NAFLD and diabetes were established using a high-fat diet and streptozocin.

#### RESULTS
The levels of fasting blood glucose (FBG), total cholesterol (TC), and triglyceride (TG) in the serum were significantly reduced after citral treatment. The levels of insulin, leptin and adiponectin were also corrected by citral treatment. Treatment with citral markedly reduced the levels of liver injury markers, malondialdehyde (MDA), alanine aminotransferase (ALT) and Aspartate transaminase (AST) and inflammatory markers like TNF-$\alpha$ and Caspase 3 and CRP levels. The expression of AMPK, LC3-II, Beclin-1 and Parkin were increased significantly, whereas mTor, ACC and NLRP3 and IL-1$\beta$ proteins were suppressed after citral treatment.

#### CONCLUSION
These results suggest that citral stimulates activity of AMPK and inhibit the NLRP3 inflammasome by enhancing the autophagy pathway in liver, which makes it a promising candidate for a therapeutic agent for the management of NASH associated with diabetes.

## PP-D-16

### HIGH EXTRACELLULAR WATER TO TOTAL BODY WATER RATIO AND DIABETIC RETINOPATHY PROGRESSION IN TYPE 2 DIABETES

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#### OBJECTIVES
Excess extracellular water is associated with chronic kidney disease progression. It is not known if it is associated with diabetic retinopathy (DR) progression. We aim to investigate the relationship between the ratio of extracellular-water to total-body-water (ECW/TBW), an indicator of fluid balance, and DR progression in type 2 diabetes mellitus (T2DM), and elucidate its role as a potential mediator in the relationship between matrix metallo-proteinase-2 (MMP2) and DR progression.

#### METHODOLOGY
We conducted a prospective study on 1,041 patients (mean age 56.5 ± 10.7 years) from the SMART2D cohort. ECW/TBW ratio was measured using bio-impedance analysis. Digital colour fundus photographs were examined for DR in a masked fashion. DR progression was defined as increase in severity across categories - normal, non-proliferative DR and proliferative DR. This research has been approved by an ethical committee.

#### RESULTS
After 7.8 years' follow-up, 15.5% of 1,041 participants experienced DR progression. Logistic regression showed that Tertile 3 ECW/TBW ratio, indicative of higher ECW/TBW ratio, was associated with 129% higher odds of DR progression with unadjusted Odds Ratio (OR) 2.29 (95% CI 1.49-3.52, p<0.001) compared with Tertile 1 ECW/TBW ratio. Having adjusted for demographics, clinical co-variables and medications, the positive association persisted for Tertile 3 ECW/TBW ratio with OR 2.79 (95% CI 1.58-4.89, p<0.001). Binary mediation revealed that ECW/TBW ratio accounted for 41.5% of the relationship between MMP2 and DR progression (p=0.001).

#### CONCLUSION
The novel finding of the association between a higher ECW/TBW ratio and DR progression highlights the importance of extracellular fluid excess as a potential marker of DR progression for future studies and interventions.