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ESKAPE pathogens – *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter species*, have been considered critical by CDC and WHO due to their high multidrug resistance observed. Non-pathogenic K-12 strain of *E. coli* is a commonly used Gram-negative model for understanding antimicrobial properties of new drug candidates and a safer relative for studying Gram-negative ESKAPE pathogens. Pathogenic strains of *E. coli* can also cause numerous issues in a multitude of environments, including severe food poisoning, UTIs, and sepsis. American Burnweed (*Erechtites hieracifolius*) is a native weed that has been used by Indigenous people for treating different conditions, but has been overlooked for many years. This study aims to investigate the antimicrobial properties of American burnweed ethanol fraction against both Gram-negative and Gram-positive bacteria. Our current results show promising inhibitory effects of American burnweed ethanol fraction against *E. coli*, showing its potential as a drug candidate. More experiments are underway to confirm the MIC, the minimum bactericidal concentrations, and to identify compounds that show inhibitory effects on *E.coli* and related pathogens.