# Optimizing Feedstock Pretreatment for Sustainable Biorefineries

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**Abstract**: Various physicochemical pretreatment methods—such as liquid hot water, acid, alkali, organic solvents, and ionic liquids—have been extensively studied to make biomass more suitable for enzymatic hydrolysis and microbial fermentation. Despite these efforts, achieving industrial-scale implementation globally has been challenging. One major obstacle is the high production cost associated with the biomass pretreatment step. After pretreatment, the biomass slurry typically requires extensive washing to remove inhibitory compounds and residual chemicals, which contributes to high water and antisolvent consumption. Simply increasing the solid loading during pretreatment can lead to ineffective results, more inhibitor formation, and high viscosity, all of which necessitate additional washing. Several methods, both physicochemical (such as membrane filtration, alkaline neutralization, ion exchange resin, liquid-liquid extraction, and activated charcoal adsorption) and biological (including laccase treatment, microbial degradation, and engineered strains), are used to detoxify the pretreated liquid fraction for enzymatic hydrolysis and fermentation. Among these, alkaline neutralization and liquid-liquid extraction are preferred due to their simplicity and low cost. Although recycling black liquor for alkali pretreatment can reduce water and chemical use, the need for alkali replenishment and the accumulation of inhibitors diminish its effectiveness. Interestingly, some studies have eliminated the water washing and solid-liquid separation steps after pretreatment with methods like liquid hot water, Tween 40, and CaO. However, there is still considerable room for future research to make biomass pretreatment more economically and environmentally viable. In the following discussion, we will explore strategies to reduce water and chemical usage, such as recovering and recycling chemicals used in pretreatment. We will also look at screening for high-tolerance enzymes and strains that can facilitate one-pot hydrolysis and fermentation without the need for solid-liquid separation and antisolvent washing. Additionally, we emphasize the importance of conducting techno-economic analysis and life cycle assessment of biorefineries to evaluate their economic and environmental impacts.