Prebiotic-Functionalised Lipid Nanocarrier Platform: Dual Approach to Mitigate Olanzapine-Induced Metabolic Dysfunction and Enhance Pharmacokinetic Stability

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Atypical antipsychotics, while crucial for treating various mental health conditions, often lead to severe side effects and unpredictable outcomes [1,2]. A key, yet underexplored factor in this challenge is the bidirectional interaction between these drugs and the gut microbiome [3]. This interplay manifests in two critical ways:

1. Antipsychotics can disrupt the gut microbiome, triggering adverse metabolic effects [3].
2. The gut microbiome can alter drug pharmacokinetics, affecting treatment efficacy [3].

These interactions not only contribute to side effects but also explain the significant variability in patient responses to antipsychotic treatments [1]. Olanzapine, a widely used atypical antipsychotic, exemplifies these challenges [4,5]. Despite its efficacy, it often induces severe metabolic side effects, including significant weight gain and microbiome dysbiosis [5]. Patients can gain up to 7% of their body weight in just 12 months, with studies showing shifts in gut microbiota favouring an obesogenic profile [5]. Gut microbiome dysbiosis subsequently disrupts olanzapine absorption, bioavailability and overall pharmacokinetic profile leading to significant inter- and intra-patient variability [4]. Such issues lead to a 73% treatment discontinuation rate, compromising efficacy and restricting access to effective therapy for many patients [6].

Recent literature has demonstrated potential for prebiotic co-administration to attenuate olanzapine-induced metabolic dysfunction, however struggle with the need for patient compliance [7]. As such, the development of an all-in-one multifunctional nanomedicine platform for optimised delivery is necessitated. This approach combines a targeted prebiotic mixture, including fructo- and xylo-oligosaccharides, with a lipid-based nanocarrier system [LPN] to strategically target the gut microbiome and 'gut-brain' axis, in order to mitigate olanzapine-induced metabolic dysfunction and enhance pharmacokinetic stability.

In vivo results indicate that the LPN platform improves treatment efficacy, tolerability, and potentially patient compliance by stabilising the gut microbial ecosystem and metabolome, countering olanzapine-induced dysbiosis. Thus, this innovative strategy not only transforms the landscape of antipsychotic therapy but also heralds a new era in drug delivery, where microbiome-targeted formulations could redefine treatment paradigms across a spectrum of challenging medications.

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