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THE ROLE OF PROBIOTICS IN MODULATING DRUG BIOAVAILABILITY

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Probiotics are live microorganisms, mainly lactic acid and non-lactic acid bacteria, as well as yeasts, and exhibit various biological activities. Lactobacillus species, such as *Lactobacillus rhamnosus* and *Lactobacillus acidophilus*, Bifidobacterium species, including *Bifidobacterium bifidum* and *Bifidobacterium lactis*, as well as Saccharomyces boulardii (a probiotic yeast) are known as common probiotic strains.

They help maintain a balanced gut microbiota, modulating its metabolic function. Moreover, live biotherapeutic products, which are a type of probiotic, may

play a therapeutic and preventive role in both metabolic and non-metabolic diseases [1, 2, 3]. Probiotics may influence drug pharmacokinetics and clinical outcomes when co-administered. They exert their effects on drug bioavailability through various mechanisms, including modification of local intestinal conditions—such as pH, transit time, and mucosal thickness—regulation of drug transport across the intestinal epithelium. Probiotic *Escherichia coli* Nissle 1917 (EcN) has been reported to improve bioavailabiliy of amiodarone probably by increasing the drug uptake through decreased intestinal pH or over-expression of the OATP2B1 transporter. probiotics may enhance the absorption of the antidiabetic drug gliclazide by increasing the activity or expression of the intestinal transport proteins MRP2 and MRP3, which mediate drug movement across cell membranes. Also, a probiotic containing *Bifidobacterium animalis* subsp. *lactis* has been reported to alter the host's gut microbiome and increase dopamine levels in the presence of L-DOPA [1, 3]. Moreover, Probiotics modulate the microbial enzymatic activity, including induction or inhibition within the gut, and alteration of drug metabolism [3, 4]. For instance, probiotics can reduce benzodiazepine toxicity when co-administered by inhibiting the enzymes responsible for the nitro reduction of these drugs [3]. Probiotics may influence drug solubility and subsequent absorption by modulating the composition of the gut microbiota and motility. By modifying intestinal transit time, probiotics can affect the re-uptake and elimination of drugs. It is worth noting that digoxin, which possesses a narrow therapeutic index, requires careful monitoring of drug levels, as certain probiotics may inhibit its inactivation and thereby increase its bioavailability [3]. Probiotics can also affect the enterohepatic circulation of drugs [1] . *In vivo* studies have shown that the probiotic *Lactobacillus casei* Shirota strain affects the plasma concentration and bioavailability of nifedipine, likely by reducing CYP3A enzyme activity in the enteric mucosa and thereby decreasing the drug's first-pass metabolism [3]. Probiotics are also correleated with pharmacodynamic of drugs. For example, they may enhance the synthesis of anti-inflammatory cytokines while suppressing pro-inflammatory ones, thereby promoting the effectiveness of medications aimed at controlling inflammation [1]. In summary, probiotics not only support gut health but also interact with drug metabolism and transport, potentially altering pharmacokinetics and therapeutic outcomes. Understanding these interactions is essential for optimising drug efficacy and safety, particularly in co-administration scenarios.

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