Virological Failure Associated with the Concomitant Use of Red Yeast Rice and Dolutegravir/Abacavir/Lamivudine in an HIV-1 Patient: A Case Report

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Abstract

Red yeast rice (RYR) is increasingly used for cholesterol management but contains monacolin K, which is chemically identical to lovastatin, and may interact with antiretroviral therapy via CYP3A4 and P-glycoprotein pathways. We report the case of a 47-year-old man with well-controlled HIV-1 infection receiving dolutegravir/abacavir/lamivudine who experienced virological rebound after self-initiating RYR supplementation. Eight weeks after starting RYR (77.7 mg daily, with a labeled monacolin K content of 3 mg), the patient developed virological rebound (897 copies/mL) despite confirmed adherence and absence of resistance mutations. Following pharmacist-led discontinuation of RYR, viral suppression (<50 copies/mL) was restored within eight weeks without modification of antiretroviral therapy. This represents the first documented case of RYR-associated virological failure in HIV treatment. Hospital pharmacists should routinely screen for herbal supplements and provide patient education regarding potential interactions with antiretroviral medications.

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Introduction

Red yeast rice (RYR) is produced by culturing the yeast Monascus purpureus on rice (Oryza sativa L.) and is increasingly utilized as an over-the-counter dietary supplement for cholesterol management, particularly among patients with statin intolerance (1). RYR naturally contains monacolin K, which is chemically identical to lovastatin, and also contains variable concentrations of other bioactive compounds that can inhibit CYP3A4 and P-glycoprotein transporters (2,3).

While antiretroviral therapy has transformed HIV infection into a manageable chronic condition, drug interactions remain a significant concern in clinical practice. The integrase strand transfer inhibitor dolutegravir, primarily metabolized by UGT1A1, may still be susceptible to interactions involving drug transporters, particularly P-glycoprotein (4). Despite the widespread use of RYR supplements and the potential for herb-drug interactions, no cases of RYR interfering with antiretroviral therapy have been documented in the literature.

This case report presents the first documented instance of virological failure in a well-controlled HIV-1 patient following self-initiated RYR supplementation. The objective of this report is to alert clinicians, particularly clinical pharmacists, to this previously unrecognized interaction and to emphasize the critical importance of comprehensive medication reconciliation that includes dietary supplements in HIV care.

Case Presentation

A 47-year-old Caucasian male with HIV-1 infection diagnosed in 2018 presented for a routine follow-up in October 2023. His medical history was significant for hypercholesterolemia and documented statin intolerance, manifesting as myalgia with both atorvastatin and rosuvastatin. The patient had no history of opportunistic infections, substance abuse, or other significant comorbidities.

Since March 2020, he has been receiving a fixed-dose

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combination of dolutegravir 50 mg, abacavir 600 mg, and lamivudine 300 mg once daily (Triumeq®, ViiV Healthcare). His adherence to antiretroviral therapy has been excellent, as assessed through monthly pill counts and pharmacy refill records, demonstrating over 95% compliance with the prescribed regimen. Regular monitoring has shown stable CD4+ T-cell counts ranging between 800 and 900 cells/mm³, with consistent viral suppression (HIV-1 RNA <50 copies/mL) for more than four years.

In August 2023, motivated by elevated total cholesterol levels (214 mg/dL), the patient independently began taking an over-the-counter RYR supplement without consulting his HIV care team. The specific product used was Bodyathlon® RYR Control Colesterol Food Supplement (5), containing 77.7 mg of Monascus purpureus fermented rice per capsule, with a labeled monacolin K content of 3 mg. The patient self-administered two capsules daily, at breakfast and dinner. He chose RYR based on internet research and marketing claims that it was a viable alternative to prescription statins.

At the routine visit in October 2023, laboratory results revealed an unexpected virological rebound, with HIV-1 RNA levels rising to 897 copies/mL—a significant increase from the previously undetectable level six months earlier. Paradoxically, the CD4+ T-cell count had increased to 960 cells/mm³ from 870 cells/mm³ at the prior visit.

During a comprehensive medication reconciliation conducted by the clinical pharmacist, the undisclosed use of RYR was identified. Adherence assessment through pill counts and pharmacy refill records confirmed over 95% compliance with the prescribed antiretroviral regimen. The patient denied any recent changes in diet (other than the initiation of RYR), concomitant medications, illnesses, or lifestyle factors that could affect treatment efficacy.

HIV-1 genotypic resistance testing, performed using population sequencing, revealed no major resistance mutations to any component of the patient's current regimen. Based on the temporal relationship between RYR initiation and virological rebound, the absence of resistance mutations, and confirmed adherence, a herb-drug interaction was suspected as the primary cause of treatment failure.

The clinical pharmacist recommended the immediate discontinuation of RYR and provided comprehensive patient education regarding the potential interactions between RYR and antiretroviral therapy.

Eight weeks after discontinuing RYR (December 2023), the viral load returned to full suppression (<50 copies/mL) without the need for antiretroviral therapy modification. The CD4+ T-cell count normalized to 710 cells/mm³. Total cholesterol remained stable at 235 mg/dL without additional lipid-lowering interventions. The patient expressed willingness to discuss alternative evidence-based lipid management strategies with his primary care physician.

Discussion

This case represents the first documented virological failure associated with concurrent RYR use in HIV treatment. The temporal relationship between supplement initiation and viral rebound, the absence of resistance mutations, confirmed adherence, and rapid viral re-suppression following supplement discontinuation provide compelling evidence for a probable drug-drug interaction, according to the Drug Interaction Probability Scale (DIPS) (6). An unexpected finding in this case was the paradoxical increase in CD4+ T-cell count (from 870 to 960 cells/mm³) concurrent with virological rebound. This dissociation between CD4 recovery and viral load control may be explained by the relatively short interval between measurements (six months) and may reflect normal physiological fluctuations in CD4 counts.

Although dolutegravir is primarily metabolized by UGT1A1 rather than CYP3A4, RYR contains multiple bioactive compounds beyond monacolin K that may affect drug transport and absorption pathways (7). While in vitro studies have demonstrated P-glycoprotein inhibition by RYR constituents, including monacolin K (2), this case paradoxically demonstrates reduced dolutegravir bioavailability despite the anticipated enhanced absorption resulting from P-glycoprotein inhibition (8,9). Several mechanisms may explain this discrepancy:

1. Biphasic effects: RYR exhibits concentration-dependent effects on P-glycoprotein, where clinical doses may induce transporter expression, while higher concentrations inhibit its activity. This biphasic dose-response pattern is also observed with other herbal products (8,10).
2. Solubility and pH effects: Dolutegravir solubility is pH-dependent (11,12). Fermentation products from RYR may alter gastrointestinal pH, reducing dolutegravir dissolution and counteracting the effects of P-glycoprotein inhibition.
3. UGT1A1 induction: Since dolutegravir is primarily metabolized through hepatic UGT1A1 glucuronidation (4,13), RYR may induce UGT1A1 activity, thereby increasing dolutegravir clearance independently of absorption changes.
4. Product variability: Commercial RYR formulations exhibit significant compositional variability beyond monacolin K content (3,7), potentially containing constituents that induce compensatory transporter expression or affect dolutegravir dissolution.

This paradoxical interaction underscores the complexity of herbal product pharmacology, where in vitro predictions may not translate to clinical outcomes (8,14).

Previous case reports have documented clinically

significant interactions between RYR and cyclosporine, resulting in elevated immunosuppressant levels and nephrotoxicity (15). Additionally, cases of RYR-associated myopathy have been reported, particularly when combined with conventional statins, suggesting that RYR may potentiate drug effects through multiple mechanisms (16). However, interactions with antiretroviral medications have not been previously described in the literature.

The variability in monacolin K content among commercial RYR products complicates the prediction of their interaction potential. Studies have shown that actual monacolin K concentrations can vary from 0.31 to 11.15 mg per recommended daily dose, which often differs significantly from labeled amounts (17). This variability, combined with the presence of other bioactive compounds, makes it challenging to establish safe dosing recommendations or predict the severity of interactions. In the present case, although the product was labeled as containing 3 mg of monacolin K per capsule, the actual monacolin K content was not chemically verified. Furthermore, the levels of other potentially interactive bioactive compounds were not quantified.

The clinical significance of this interaction extends beyond the individual case. Even temporary virological rebound increases the risk of developing drug resistance and may compromise long-term treatment outcomes. In regions with limited access to alternative antiretroviral regimens, such interactions could have serious public health implications.

A notable limitation of this case is the absence of plasma antiretroviral drug level measurements, which would have provided pharmacokinetic evidence of altered dolutegravir absorption or clearance. Additionally, the lack of chemical analysis of the specific Bodyathlon® RYR product used prevents definitive quantification of the actual bioactive compound content.

This case highlights the critical role of clinical pharmacists in HIV care and demonstrates the importance of comprehensive medication reconciliation that specifically includes dietary supplements. Many patients perceive dietary supplements as inherently safe and may not disclose their use to healthcare providers (18). In cases of paradoxical interactions, immediate discontinuation of RYR is recommended for patients experiencing unexplained virological rebound, along with enhanced viral load monitoring and consideration of alternative lipid-lowering therapies.

Conclusion

This report represents the first documented case of RYR-associated virological failure in HIV treatment. The pharmaceutical care model emphasizes the pharmacist's responsibility to identify potential drug interactions and provide patient education to optimize therapeutic outcomes. Hospital pharmacists should routinely screen for herbal supplements and provide patient education regarding potential interactions with antiretroviral medications.

Conflict of Interest:
None declared.

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