



# Ashwagandha-Induced Gastric Upset in Post-Covid Patient-A Case Report and Brief Review of the Literature

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## Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

## Article Information

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Case Report

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## ABSTRACT

Adverse drug reporting of herbal drugs is less common as they are generally considered as safe. It is also very common to use self-medication by people in the case of herbal drugs. But many times, mild to severe events have been seen with the use of herbal or ayurvedic medicines. We have reported a case of post-covid patient, who was having complained of headache, body ache, lethargy, backache, generalized weakness and excessive sweating since one week. Patient had past history of hospitalization due to COVID-19 moderate pneumonia one month back. Patient also had history of type-2 diabetes mellitus, hypertension and dyslipidemia and was taking anti-diabetic and anti-hypertensive medications continuously. Ashwagandha powder (*Withania somnifera*), Maha yogaraj guggulu (herbal anti-inflammatory) and Syrup Amynity Plus (herbal immune-booster) were prescribed for these complain. Conversely, moderate severity adverse reaction like nausea, vomiting, diarrhea, and abdominal cramps were noted after the intake of suspected drug i.e. ashwagandha powder. Nevertheless, symptoms were relieved after the de-challenge. This shows a temporal relation of the event with the suspected drug. One more possibility of drug-drug interaction in this case

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cannot be ruled out completely. Causality assessment was done for this adverse event and it was considered as the “probable” category of the adverse event in WHO causality classification.

**Keywords:** Adverse drug reaction; pharmacovigilance; ashwagandha; withania somnifera; case report.

## 1. INTRODUCTION

*Ayurveda* is an ancient treasure of herbal medicine in India and is being practiced here since about 2500 years back. It is an estimation that 80% of Indian population is using *ayurvedic* medicine in some form [1]. *Ayurveda* is also being popular in western countries as well. It is a general perception that herbal drugs are quite safe and do not produce any side effect. However, there is paucity in adverse drug reaction (ADR) reporting for herbal or *ayurvedic* drugs to pharmacovigilance authorities. Few studies published have shown that serious adverse reactions may happen due to herbal medicines [2,3,4,5,6]. *Ashwagandha* (*Withania somnifera*) is an ayurvedic medicine possesses anti-inflammatory, anti-tumor, anti-stress, antioxidant, immunomodulatory, hemopoietic, and rejuvenating properties [7]. Few authors have also reported some serious ADRs due to ashwagandha [8,9,10]. *Ashwagandha* has been found effective herbal remedy in covid and post-covid patients' also [11]. Here, we are reporting a case of *Ashwagandha* powder induced moderate gastric upset in a post covid patient. *Ashwagandha* powder was prescribed her for the post-covid symptoms of lethargy, body ache and generalized weakness.

## 2. CASE PRESENTATION

A 56 year old female patient of *kaphaj prakriti* (*Ayurvedic bodily constitution*), body weight 62 kg (BMI 25.8 kg/m<sup>2</sup>) came in OPD with the chief complaints of headache, body ache, lethargy, backache, generalized weakness and excessive sweating since last one week. She had a history of COVID-19 infection one month back, with moderate pneumonia, hospitalized for 10 days and also developed herpes zoster rashes in her left side of the abdomen. At that time, she was not having any sign of COVID-19. She also had history of type-2 diabetes mellitus, hypertension and dyslipidemia since last 12 years and she was taking anti-diabetic and anti-hypertensive medications continuously. She had also history of known drug allergies with ampicillin, amoxicillin and ibuprofen tablets.

### 2.1 Intervention

For her post covid complains of generalized body ache and weakness, she was prescribed *ashwagandha powder* (*Withania somnifera*) 3gm twice a day orally with milk, *Maha yogaraj guggulu* (herbal anti-inflammatory) 2 tablets twice a day and *Syrup Amynity Plus* (sugar-free immune modulator herbal preparation of aimil pharma) 10 ml twice a day orally with water was advised on 17-06-2021.

### 2.2 Adverse Drug Event

Patient had started taking the above prescribed medication from the evening of 17-06-2021. Since next day morning she felt discomfort in stomach and mild sensation of nausea. Gradually, the condition worsened during same night after taking prescribed evening dose. Frequent diarrhea and vomiting with moderate severity started with abdominal cramps since midnight. She tolerated these symptoms to some extent till early morning and then she took oral rehydrating solution by herself. Then, she got some relief and slept.

### 2.3 Preventive Medication

The case was presented in OPD next morning. She was advised to withhold *ashwagandha powder*. For the presenting complains *kutajghan vati* (*Holarrhena antidysenterica* extract and *Aconitum heterophyllum* powder) was prescribed for next three days. *Maha yogaraj Guggulu* 2 tablets and *Syrup Amynity Plus* 2 tsp twice a day with water was continued. She got complete relief within same day. Her written consent was taken for documentation and publication of this case report. This Adverse drug reaction (ADR) reporting was also done in prescribed format to National Coordination Centre (NCC), Pharmacovigilance program of India (PvPI), Indian Pharmacopoeia Commission (IPC), Gaziabad, U.P. and to Coordinator, Suspected Adverse Reactions National Pharmacovigilance Program for Ayurveda, Siddha, Unani and Homeopathy drugs (ASU & H Drugs), National Pharmacovigilance Coordination Centre (NPvCC), Sarita Vihar, New Delhi through e-mail

on 28<sup>th</sup> June, 2021 and both of them acknowledged as well.

### 3. DISCUSSION

We hereby illustrated a case report of adverse drug reaction after consuming *Ashwagandha* in crude root powder form. We observed a positive de-challenge and temporal association between adverse event and suspected herbal drug. On taking *Ashwagandha* powder of the same batch by other patients also, no such adverse event was observed. This indicates the susceptibility of the patient toward the reaction with this particular drug. As far as our clinical experience in post-covid sequel cases suggests that *ashwagandha* powder has an excellent adaptogenic/anti-stress, anti-inflammatory, anti-arthritis and immune booster properties.

Causality assessment was done by WHO-Uppsala Monitoring Centre Causality Assessment Scale, Severity Assessment using Hartwig's Scale and Naranjo's ADR Probability Scale. WHO-UMC causality category was probable/likely, Hartwig's Scale Severity score was 3 (moderate) and Naranjo's ADR Probability Scale was 5 (probable ADR) with *Ashwagandha* administration. This ADR can be classified as Type A- Augmented reactions as per the Wills and Brown classification. Outcome of this present event was full recovery of patient (Please see, Table 1. Naranjo ADR probability scale—items and score and Table 2. Severity Assessment using Hartwig's Scale. 3).

*Ashwagandha* is believed to be a quite safer drug. It may be possible that in this particular post covid case, drug may interact in different way in the due course of treatment. There is also a remote possibility of higher dosage form as patient was also under stress at that time due to prolong hospital stay during covid illness. Only after the re-challenging technique we can draw any firm conclusion. In this case, the re-challenging technique was not followed due to the patient discomfort and ethical issues.

Few authors have reported adverse effects of *Ashwagandha* such as thyrotoxicosis [12] and jaundice leading to severe intra-hepatic cholestasis [13], while many other studies are only in favor of mild adverse events. These side effects are still uncommon and have not been

clearly reported. Gastrointestinal upset, diarrhea, nausea and vomiting are seen with higher dosage form most probably due to direct irritation to the intestinal mucosa [14]. In a randomized controlled trial conducted among 92 patients of osteoarthritis of knee joint treated with a poly-herbal combination containing *ashwagandha* shown mild and uncommon side-effects and no change in ALT and AST levels [15]. Rheumatoid arthritis was treated by other group with *ashwagandha* and *Sidh Makardhwaj* in a prospective pilot study demonstrates that symptoms were improved without any alteration in liver enzymes level [16]. In a study conducted by Choudhary et al, tolerability of *ashwagandha* was found excellent and remarkable improvements were seen in cognitive parameters as compared to placebo among fifty adults without any sign of hepatotoxicity or ALT/AST elevations [17]. There were few uncommon or mild adverse effects observed in a double blind randomized clinical trial among chronic stress patients treated for eight weeks with *ashwagandha* root extract [18]. In another prospective, randomized double-blind, placebo-controlled study in stress and anxiety patients by other group, 30 patients were enrolled in *ashwagandha* treated group, out of which 20% cases were having mild side effects like nasal congestion, cough and cold, constipation, poor appetite and sleepiness [19]. Verma et al claims *Ashwagandha* root extract safe in normal healthy individuals without any change in thyroid hormonal profile. They did not found any adverse event in any participant during eight week randomized, placebo-controlled study [20].

We have first ever reported this type of adverse drug reaction after ingestion of *ashwagandha* in post-covid patient. However, it is recommended by Ministry of AYUSH (Ayurveda, Yoga & naturopathy, Unani, Siddha and Homeopathy) in post-covid cases as a rejuvenator or general tonic for improving post-covid sequel of health deterioration [21]. It may be possible that this reported event may be due to more irritation to gastro-intestinal mucosa or due to alteration in gut flora or due to immune-compromised condition in this particular case. As the patient was having type-2 diabetes mellitus, hypertension and dyslipidemia, and was on regular medications for these problems, the chances of Herb-Drug reaction cannot be ruled out.

**Table 1. Naranjo ADR probability scale—items and score**

Question	Yes	No	Don't know
Are there previous conclusion reports on this reaction?	+1	0	0
Did the adverse event appear after the suspect drug was administered?	+2	-1	0
Did the AR improve when the drug was discontinued or a specific antagonist was administered?	+1	0	0
Did the AR reappear when drug was re-administered?	+2	-1	0
Are there alternate causes [other than the drug] that could solely have caused the reaction?	-1	+2	0
Did the reaction reappear when a placebo was given?	-1	+1	0
Was the drug detected in the blood [or other fluids] in a concentration known to be toxic?	+1	0	0
Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	+1	0	0
Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	+1	0	0
Was the adverse event confirmed by objective evidence?	+1	0	0
<b>Total Score</b>			<b>5</b>

Scoring for Naranjo algorithm: >9 = definite ADR; 5–8 = probable ADR; 1–4 = possible ADR; 0 = doubtful ADR.

N.B. 1. Scoring for Naranjo algorithm: 5 (5–8 = probable ADR)

2. Drug was not re-administered, placebo was not given, blood concentration not performed, dose was not increased or decreased and not assessed by any objective evidence.

**Table 2. Severity Assessment using Hartwig's Scale. 3**

Level	Description
1	An ADR occurred but required no change in treatment with the suspected drug.
2	The ADR required that treatment with the suspected drug be held, discontinued, or otherwise changed. No antidote or other treatment requirement was required. No increase in length of stay (LOS)
3	The ADR required that treatment with the suspected drug be held, discontinued, or otherwise changed. And/ or An Antidote or other treatment was required. No increase in length of stay (LOS)
4	Any level 3 ADR which increases length of stay by at least 1 day. Or The ADR was the reason for the admission
5	Any level 4 ADR which requires intensive medical care
6	The adverse reaction caused permanent harm to the patient
7	The adverse reaction either directly or indirectly led to the death of the patient

[Mild= level 1 and 2, moderate= level 3 and 4, severe= 5, 6 and 7].

The suspected ADR found to be moderate on Hartwig's severity scale assessment.

#### 4. CONCLUSION

With only this case report, we cannot come to a conclusion that use of *ashwagandha* powder in post-covid patients can cause adverse effects. We have reported that already the patient was suffering from so many health issues. By taking *ashwagandha* powder, suddenly she becomes too sick. She was taking other medication also, so there is likely to be a remote possibility of drug-drug interaction in this particular case. World Health Organization also has suggested

that post-covid patients generally up to one year clinically may suffer from one or other symptoms as well. However, on the basis of this present case report, we can recommend that use of *Ashwagandha* should be done cautiously especially in covid cases or immune compromised cases. It may present unpredictable adverse event.

#### DISCLAIMER

The products used for this research are

commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

## CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the authors.

## ETHICAL APPROVAL

It is not applicable.

## NOTE

The study highlights the efficacy of "Ashwagandha" which is an ancient tradition, used in some parts of India. This ancient concept should be carefully evaluated in the light of modern medical science and can be utilized partially if found suitable.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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