



Asian Journal of Pharmacognosy

Toxicological Report

Case report: Possible drug interactions between antidiabetic allopathic drugs and herbal products

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While allopathic medicine is the preferred medicine of a large section of the Bangladesh population, various traditional medicine systems also are functional in Bangladesh, the chief among them being Ayurveda, Unani and homeopathy. These traditional medicinal systems rely mostly on plant-based medications, particularly Ayurveda and Unani. Both urban and rural people often combine allopathic medications with one or other of the traditional medicine systems or even home remedies or folk medicines, which are also essentially plant-based. As a result there is an enormous amount of anecdotal evidence or adverse interactions when a traditional medicinal drug is taken along with an allopathic drug. This is because while an allopathic drug often consists of a single active ingredient, a traditional medicine or plant-based drug may contain decoction or extract or fermented product of one or more plants, which in reality means taking hundreds of phytochemicals along with a single allopathic drug ingredient. Thus there is always a strong possibility of interactions between allopathic and traditional drugs (herb-drug interactions), and which interactions may be adverse. A review conducted in 2007 found that St. John's wort was the most common herbal drug in adverse interactions, while the most common allopathic drug adversely interacting with herbal drugs was warfarin (Gohil and Patel, 2007). Induction of mania has been reported in depressed patients who mixed antidepressants with *Panax ginseng* (Fugh-Berman, 2000). Elderly patients may be more vulnerable to herb-drug interactions (Kafeel, 2016). Diabetes is a common disorder throughout the world and is rising at a rapid rate, possibly because of changes in lifestyle (more sedentary lifestyle) and changes in food habits (like eating refined sugar more often). The disease is characterized by elevated blood glucose levels. Oxidative stress is increased during diabetes leading to more serious complications like cardiovascular disorders, diabetic retinopathy, diabetic neuropathy, and diabetic nephropathy. Existing allopathic drugs cannot cure the disease but can reduce elevated blood glucose levels. In Bangladesh, the number of diabetic patients has risen in recent years (Biswas et al., 2016; Zaman et al., 2016). Patients in rural and urban slum areas lack access or affordability to allopathic blood glucose lowering drugs and find insulin injections to be cumbersome. Even literate affluent diabetic persons are prone to use traditional medications on the side of allopathic drugs. In this case report, we are reporting on possible adverse herb-drug interactions in two diabetic patients who have used traditional medications (herbal preparations) along with allopathic blood sugar lowering drugs.

Case 1:

Patient is male, currently 63 years in age, literate, affluent and lives in Dhaka city, Bangladesh. Type 2 diabetes was diagnosed in 2010. As per advice of his allopathic physician, he took metformin (500 mg) once daily from 2010 till 2012. From January 2013, again as per advice of his allopathic physician, he



started taking twice daily (morning and evening) vildagliptin (50 mg) plus metformin (850 mg). Patient did not suffer from any ill effects during taking of these drugs. From June 2015, the patient, on his own initiative, started taking along daily with the allopathic drugs, 4-5 teaspoonfuls of fresh juice squeezed from leaves of *Tinospora cordifolia* in the morning. [*T. cordifolia* is regarded as a very effective plant by Bangladesh and Indian traditional medicinal practitioners for lowering blood glucose.] In February 2016, the patient suddenly felt mild irritation in both eyes. In subsequent days, his vision gradually became more and more hazy but he continued *T. cordifolia* till July 2016. He then went to see an allopathic eye doctor and was diagnosed with massive bleeding through multiple ruptures in both eyes. The patient was operated upon but has regained only partial vision as of to date. The massive bleeding in both eyes can be due to interactions of any or both allopathic antidiabetic drugs (vildagliptin, metformin) with *T. cordifolia* leaf extract. However, whole plant powder as well as decoction of leaves and stems of *T. cordifolia*, administered to mice for 15 days, did not have any toxic effects at doses up to 8g per kg body weight and 9 ml per kg body weight, respectively (Pingale, 2011). Vildagliptin has no reports of serious adverse toxic effects (Ligueros-Saylan et al., 2010) and certainly no cases of causing bleeding within the eyes when taken by itself or with metformin. Metformin can cause lactic acidosis, but usually from over-dosage.

Case 2

Patient is male, currently 65 years in age, literate, affluent and lives in Nilphamari town in Nilphamari district, Bangladesh. He was diagnosed with Type 2 diabetes in 2010 and advised by his allopathic doctor to take 4 mg glimepiride and 50 mg sitagliptin twice daily, in the morning and evening. In 2015, he also started taking with the allopathic drugs, an herbal product (powder form) for diabetes, which was not approved by the Drug Administration of Bangladesh and was manufactured locally. According to the manufacturer's specifications on the product, 5-10 g of the powder was to be suspended in normal or warm water and taken twice daily in the morning and evening on an empty stomach. The said powder was supposed to contain (in dried and powdered form) cloves of *Allium sativum*, fruits of *Swertia chirata*, fruits of *Momordica charantia*, fruits of *Emblica officinalis*, seeds of *Syzygium cumini*, leaves of *Ginkgo biloba*, fruits and seeds of *Zizyphus mauritiana*, roots of *Opuntia dillenii*, seeds of *Siceraria lagenaria*, and bark of *Azadirachta indica*. The manufacturer claimed that the powder can completely cure diabetes after taking orally for about 2 months. However, taking the herbal powder along with the allopathic drugs caused severe diarrhoea with bloating and cramps after just 2 days of taking the herbal powder. The diarrhea and other symptoms persisted for about 15 days and slowly went away with time. The herbal powder was not taken by the patient alone; however, the powder in its manufacturer prescribed dose and mode of administration in warm or normal water was done by the authors on a voluntary basis for 3 days. The authors did not suffer from any ill-effects and certainly not diarrhoea or any other form of gastrointestinal disorders. In this context, it may be noted that the various ingredients within the herbal powder, with the exception of *Ginkgo biloba* are commonly used in Bangladesh, alone or in various combinations for lowering blood glucose in folk medicinal, Ayurveda, and Unani preparations, and have been so done for possibly hundreds of years. So the effects on the patient may be considered a case of herbal-allopathic drug interactions.

Declaration of Conflict of Interest

No conflict of interest associated with this work.

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Asian Journal of Pharmacognosy (2017) 1(2):33-35

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