



EXTRACTION OF CAFFEINE AS HERBAL ALTERNATIVE OF ISONIAZID AND IT'S PERSONALIZATION BASED ON POLYMORPHISMS IN DNA SEQUENCE

DAYADHAR DIKSHIT*

Department of Chemistry, Pt. L. M. S. Govt. (Autonomous) P.G. College, RISHIKESH – 249201 (Uttarakhand) INDIA

(Received : 15.12.2012; Accepted : 22.12.2012)

ABSTRACT

Natural herbs are nothing more than plants made by the God, with infinite intelligence. Therefore herbal medicines may contain various ingredients other than active component which may be chemically similar or able to enhance the potency of active component. In light of above view the extraction method is also play an important role in effect of herbal drug. Furthermore experiences show that for the same drug people may respond well, badly, or not at all. Currently doctors diagnosis the disease and prescribe medicine on the basis of external symptoms and blood report of the patient. It some times results adverse effect, overdose of medicine. Adverse drug reaction accounted for 2.2 million hospitalizations and over 1,00,000 deaths in USA in 1994¹. Currently there is no simple way to determine whether people will respond well, badly, or not at all to a medication. Pharmacogenomics² deals with the influence of genetic variation on drug response in patients by correlating gene expression or single nucleotide polymorphism with a drug's efficacy or toxicity. Therefore it provides a revolutionary pathway to diagnosis the disease and prescribes "Personalized" medicine on the basis patient's genotype. Genetic variation in drug receptors can have a profound effect on drug efficacy. It has been already reported that variation in sequence of amino acid in DNA directly affects the response of β_2 – adrenoreceptor to β_2 – agonists^{3,4}.

In this paper, we discussed polymorphism in DNA and its effect on synthesis of drug metabolizing enzymes in human beans and other organism and it's use to determining the doze of alternative herbal drugs for patient along with benefits, challenges and various research scope in pharmacogenomics.

Key words: Pharmacogenomics, Polymorphism, β_2 – agonists, Alternative herbal drug.

INTRODUCTION

Herbal medicines are a part of traditional Chinese medicine (TCM); Ayurveda, and other healthcare systems such as homeopathy. Herbal drugs are considered as less potent than prescribed medicines. The latter usually contain one highly concentrated active ingredient, while herbs may have several active ingredients that are chemically similar. Herbal ingredients work synergistically to contribute to, or detract from, the therapeutic effect of each individual ingredient, therefore they have no harmful side-effects. The man-made, synthetic drugs stop, block or replace a bodily function while herbs work with the body's natural functions. Man-made drugs usually work on relieving the "symptoms" of a disease, whereas herbs work on the cause of the disease. Since herbs are natural, they are more readily absorbed and assimilated by the body. Since man-made drugs are unnatural, the body doesn't recognize them, so only a small amount are actually absorbed and assimilated. Whether human-made or natural, the most important criteria for a medicine's use

is safety, effectiveness and quality: identity, purity, potency and stability. Therefore drug dose is also an important matter of discussion and research. Currently doctors diagnosis the disease and prescribe medicine on the basis of external symptoms and blood report of the patient and there are no simple way to determine whether people will respond well, badly, or not at all to a medication. Therefore pharmaceutical companies are developing drugs using a "one size fits to all" system. Latest researches show that inter individual differences in drug response is also depends on variation in gene encoding drug-metabolizing enzymes, drug transporters or drug targets⁵⁻⁸. It has been already reported that variation in sequence of amino acid in DNA directly affects the response of β_2 – adrenoreceptor to β_2 – agonists⁷⁻⁸.

Single nucleotide polymorphism and its effect on drug response

A Single Nucleotide Polymorphism, or SNP, is a small genetic change, or variation, that can occur within a person's DNA sequence. More than 1.4 million SNPs were identified in initial sequencing of human genome.

The genetic code is specified by the four nucleotide, A (adenine), C (cytosine), T (thymine), and G (guanine). SNP variation occurs when a single nucleotide, such as an A, replaces one of the other three nucleotide letters-C, G, or T. The alteration of the DNA segment AAGGTTA to ATGGTTA, where the second "A" in the first snippet is replaced with a "T". If SNPs found within a coding sequence are of particular interest to researchers because they are more likely to alter the biological function of a protein.

For example:

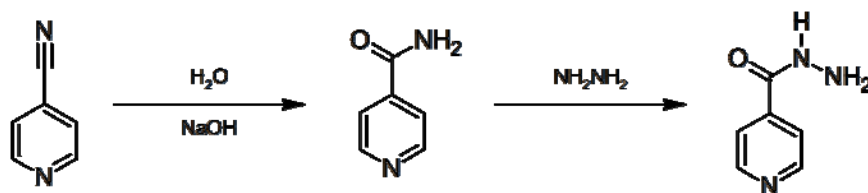
1. Variation in sequence of amino acid in DNA directly affects the response of β_2 -adrenoreceptor (a gene product) to β_2 -agonists (medicine) in humans.
2. Variation in sequence of amino acid in DNA that code CYP450 enzymes can influence their ability to metabolize certain drugs. Less active or inactive forms of CYP enzymes can cause drug overdose in patient.
3. The enzyme; MRD-1 acts on anticancer drugs and decreased response in HIV Infected patients, therefore high dose of medicine is required for such patients
4. Gs protein α acts on β -lockers such as metoprolol and results in antihypertensive effect.
5. The enzyme; N-acetyltransferase (NAT2) acts on Isoniazid, caffeine and sulfonamides drugs and make patients, Hypersensitivity for these drugs therefore even low dose of medicine effects as over dose.

Similarly SNP influence various other enzymes and hence drug response. Beside these enzyme drug transport proteins also affected by SNP and influence various drug response. They provide protective functions (Blood-brain barrier), contributing to critical cellular processes and Influence drug absorption from small intestine.

Alternative herbal drugs

Caffeine

Caffeine is reliable herbal alternative of synthetic drug, Isoniazid. Isoniazid (Laniazid, Nydrazid) is, also known as isonicotinylhydrazine (INH), is an organic compound that is the first-line medication in prevention and treatment of tuberculosis. Isoniazid is available in tablet, syrup, and injectable forms (given intramuscularly or intravenously and may be prepared by the base hydrolysis of 4-cyanopyridine to give the amide, followed by displacement of ammonia by hydrazine⁹.



This medicine causes very serious liver disease. Therefore the effect of its herbal alternative 'Caffeine' along with polymorphism in DNA sequence is subject matter of discussion.

EXPERIMENTAL

Extraction of tea caffeine

Tea caffeine can be extracted by microwave-assisted extraction (MAE) method. The experimental conditions can be changed to investigate the maximum extraction of tea caffeine as well as the other ingredients. For this purpose concentration of solvent such as ethanol can be change from zero to hundred percent. Similarly other parameters such as liquid/solid ratio and extraction time may be vary to investigate the efficiency and quantity of the drug. Various experimental conditions and extent of extraction is shown in Fig. 1-3.

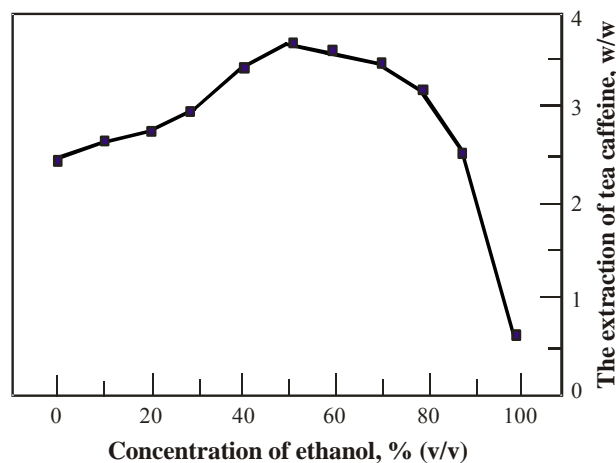


Fig. 1: Effect of ethanol concentration in water on the extraction of tea caffeine

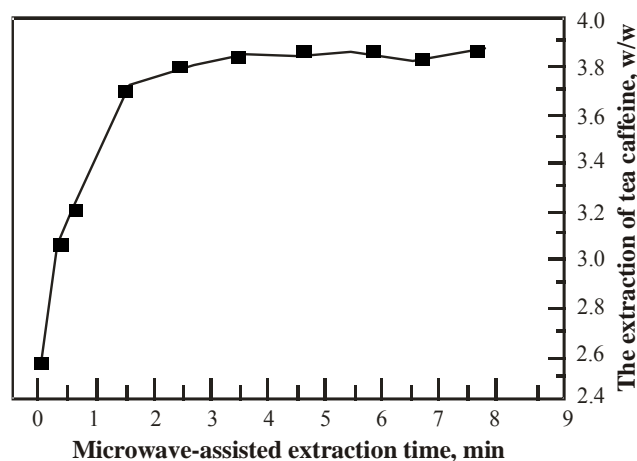


Fig. 2: Effect of extraction time on the extraction of tea Caffeine

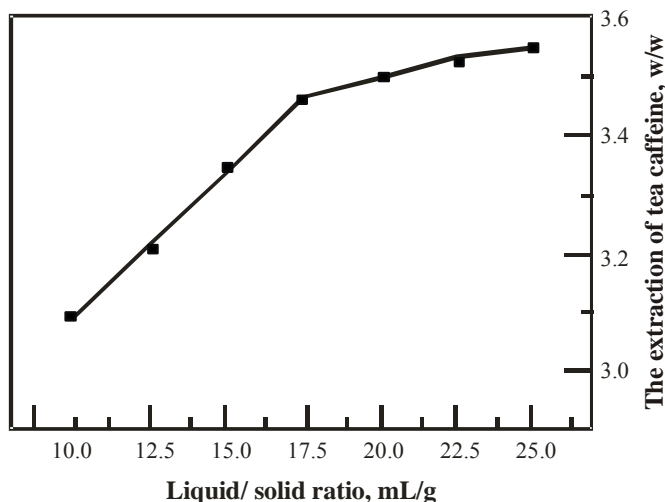


Fig. 3: Effect of liquid/solid ratio on the extraction of tea caffeine

RESULTS AND DISCUSSION

To determine the effect of ethanol concentration, 5 g of green tea leaves are extracted by MAE method for about 5 min. The liquid/solid ratio in these experiments is maintained upto 20 : 1 mL g⁻¹. Similarly to determine the effect of extraction time on the extraction of tea Caffeine 5 g of green tea leaves are extracted by MAE method with the liquid/solid ratio 20 : 1 mL g⁻¹ and ethanol/water ratio (1 : 1 v/v). It has been observed that extraction of tea caffeine with MAE for 4 min (4%) is higher than those of extraction at room temperature for 20 h, ultrasonic extraction for 90 min and heat reflux extraction for 45 min (28 and 3.6%), respectively. Thus MAE was more effective than the conventional extraction methods studied.

Ephderine

It is reliable herbal alternative drug of β_2 -agonists⁷, it includes Clenbuterol and Salbutamol. Medically these drugs are used to reduce the symptoms caused by asthma.

ACKNOWLEDGMENT

I acknowledge my sincere thanks to Dr. T Singh (Research Guide), Prof. Baccha Singh (B. H. U.), Prof. P. K. Mishra (B.H.U), Prof. Jagdamba Singh (Allahabad Univ.), Dr. S. K. Dabral, H. O. D, Dept. Chem. (P. L. S. P.G. College, Rishikesh).

REFERENCES

1. J. Lazarou, B. H. Pomeranz and P. N. Corey, JAMA, **279(15)**, 1200 (1998).
2. J. E. Staunton, D. K. Slonim, H. A. Coller et al., Proc. Natl. Acad. Sci. USA., **98**, 10787 (2007).
3. S. B. Liggett, Am. J. Respir. Crit. Care. Med., **161**, S 197 (2000).
4. J. O. Khatri, Pharma. Times, **11**, 28 (2006).
5. W. E. Evans and H. L. McLeo, N. Engl. J. Med., **348**, 538 (2003).
6. W. E. Evans and M. V. Relling, Science, **286**, 487 (1999).

7. P. E. Carson, C. L. Flanagan, C. E. Ickes and A. S. Al-ving, *Science*, **124**, 484 (1956).
8. W. E. Evans, *Gut.*, **52ii**, 10 (2003).
9. T. P. Sycheva, T. N. Pavlova and M. N. Shchukina, Synthesis of Isoniazid from 4-cyanopyridine, *Pharmaceut. Chem. J.*, **6(11)**, 696-698 (1972).