

## Potential Scope of Multivariate Analyses in Herbal Therapeutics of Diabetes Mellitus

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Diabetes, which often occurs with hypertension and hyperlipidaemia as part of metabolic syndrome is characterized by hyperglycaemia. It is a devastating health problem due to modern lifestyle especially in developing and developed nations. According to National Diabetes Statistics report, 34.2 million or 10.5% of United States population had diabetes in 2018 [1] with the global prevalence expected to reach 642 million by 2040 [2]. There are many pharmaceutical preparations of synthetic nature to treat T2DM to a certain extent but safer, more effective and cheaper management approaches are needed [3,4]. Herbs are increasingly popular to fulfil this need which has often raised questions pertaining to safety and efficacy due to multicomponent nature of herbals [3,5]. The multicomponent could mean the diverse chemical compounds in the herbs such as flavonoids, triterpenes, alkaloids etc in a particular herb numbering up to thousands [6] or herbal preparations themselves could have up to ten individual herbs [7]. The advances in information and computer technology in recent times has provided powerful computers as well as algorithms having capabilities to deal with multivariate or large data from such samples.

The data generated could be from HPLC profile of the herbs [8] but Fourier Transform Infrared (FTIR) spectroscopy [9] has one major advantage, which is the negation in the need for internal standards. The approach of metabolite fingerprinting involves the use of multivariate or chemometric analyses to classify or cluster samples and is best combined with FTIR spectroscopy, that has the advantage of being a relatively simple and cheap approach [10,11]. The latter referred paper differentiated three closely resembling and three morphologically distinct species from the genus *Phyllanthus* whereas other works have differentiated plants from the genus *Ficus* or *Melastoma* according to locations [12].

The use of metabolite fingerprinting or chromatography of herbs are basically to determine their quality. Although, basically the fastest and simplest way to establish identity and quality of plant materials is by visual inspection of size, shape, color and texture characteristics [13], until recently this could be done only by a subjective manner. Often, plants are identified commonly by leaf and next by flowers, etc but plants from same family share similar characteristics [14]. Examples of some common herbs are the species from the genus *Phyllanthus* spp [15,16] and *Melastoma* spp. [17] which, requires a botanist to identify them. Image analysis which is a multivariate analysis can be carried to facilitate herbal identification without the need for specialized botanical knowledge (except the initial identification of images used for 'calibration sample'). These images can be then compared with the images that are to be classified. This field which is known as computer vision and the approach of convolution neural network (CNN) is often used [18] to extract features from images and classify herbs [19,20].

In the case of herbals, the quality of herbal preparations is also related to their efficacy. The herbal preparations should also exhibit minimal or no side effects. It is our opinion that these could be best achieved by combining few herbals with similar herbal activity. It is suggested to combine up to four herbs and a potential combination for antidiabetic activity could be *Orthosiphon stamineus*, *Melastoma malabathricum*, *Andrographis paniculata*, with *Phyllanthus niruri* as a fourth option or without it. The choice of these species is because they have been reported to possess antidiabetic activity or are present in some herbal preparations for antidiabetic, or other related beneficial effect.

Various authors report beneficial antidiabetic effect of the suggested herbals [21-23] or their isolated compounds [24,25]. Other than having various reports on its activity, the genus *Phyllanthus* is often used in herbal formulations. For example, *P. niruri* is present in a polyherbal formulation named Diabecon whereas a related species, *P. emblica* is present in Glycoherb [26,27]. Both of these formulations are for diabetes. *Andrographis* is also commonly present in polyherbal preparations and is labelled as having beneficial hepatoprotective effect [28], whereas *O. stamineus* is commonly used as java tea but some herbal formulations of it are available [29]. Another reason in the choice of plants is that they also contain certain unique chemicals such as andrographolide which is easily isolated and sinensetin that can allow fine tuning of activity when combined with multivariate analysis.

The preparation of new herbal formulations of these herbs will benefit from prior research and usage of the herbs. The herbs are commonly available and grow easily. The usage of leaves or aerial parts mean sample collection can be done easily and initial quality control can use image analysis as it is a cheap technique. The chemical content of the individual herb or combined can be initially carried out with FTIR metabolite fingerprinting and later with chromatography and the chromatographic pattern analysed by multivariate analysis.

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