INTRODUCTION
An individual response to a drug depends on many factors such as genetics, age, gender, environment and disease. The racial background is another important contributor of a person's capability to clear drugs and/or other exogenous compounds from the body. Polymorphism exhibited by drug-metabolising enzymes are well known and have been investigated for many years. Recently, the exploding field of pharmacogenetics has focussed not only on the characterization of enzymes responsible for drug biotransformation, but also, on describing the various sources of variability in enzyme activity.

Genetic polymorphism have been revealed in many drug metabolizing enzymes, which lead to wide range of enzymatic activities and established at least two phenotypes in a population. While initial observations and studies focussed on populations of Caucasian origin, reports from other populations followed. The incidence of poor or slow metaboliser phenotype for a given enzyme caused by allelic variants may vary significantly between populations\(^1\).

\textit{CYP2D6} polymorphism is one of the well-characterized and clinically significant polymorphisms of drug oxidation. This defect has been shown to be responsible for pronounced inter-individual variation in the metabolism of many clinically important drugs. Indeed, recent estimates suggest that \textit{CYP2D6} may be responsible for the metabolism of up to 25% of all prescribed drugs\(^-\).
Since \textit{CYP2D6} substrates are structurally diverse, they can perform different pharmacological effect. Inter-individual variation in drug metabolism as a result of aberrant \textit{CYP2D6} expression can influence both drug pharmacokinetics and pharmacodynamics, thereby producing a variety of pharmacological consequences. The individuals who do not have functional \textit{CYP2D6} protein are unable to metabolize compounds that are \textit{CYP2D6} substrates. In contrast, subjects with multiple functional \textit{CYP2D6} protein with enhanced enzyme activity will metabolize the \textit{CYP2D6} substrates rapidly. Moreover, certain reactions catalysed by \textit{CYP2D6} result in the conversion of a prodrug that is inactive, or has only minimal activity, to its active form. Poor metabolizing individuals (PM) are unable to perform this metabolic conversion and therefore do not obtain the desired therapeutic effect.

Inheritance of certain \textit{CYP2D6} allelic variants has also been associated with altered susceptibility to Parkinson’s disease and several types of cancer\textsuperscript{3}. Thus determination of these genetic polymorphism may be of clinical value in predicting adverse or inadequate response to certain therapeutic agent and in predicting increased risk of environmental or occupational exposure-linked disease.

There are marked differences in both \textit{CYP2D6} genotype and phenotype in populations of different racial origin. The most striking difference in PM frequency is seen between Caucasian and Oriental populations\textsuperscript{4}. On average, the PM frequency
in the Caucasian population is 7% and it remains constant in most Caucasian population studied\(^5\). However, most of the Chinese and Japanese population showed a PM frequency of <2\(^\%\)\(^6\). In contrast, conflicting results observed in Africans. In Africa, the incidence of PM ranged from 0 to 19\(^\%\) and appeared to be dependent on the probe drug used\(^7\). Since most investigations are focused on subjects of defined ethnic origins, pharmacogenetic information concerning populations subject to ethnic admixture ("melting-pots" such as "North America") is generally not available. Ethnic diversity constitutes both a challenge and an opportunity to prudently apply pharmacogenetics, so that variability in both drug disposition and effect may be better understood.

The Indian population is polygenetic, and the people of India can be classified under different ethnic group. Very little information was available regarding the \(CYP2D6\) polymorphism in Indian population when the present study was initiated. However, later on studies are reported with North Indian population\(^8\) and Hyderabad City population of South India\(^9\). Since this polymorphism has not been studied extensively in all the South Indian states, the present study was undertaken.

Phenotyping or genotyping is used to assess individual \(CYP2D6\) activity. The direct measurement of the activities of drug-metabolizing enzymes, i.e. phenotyping, is usually done by measuring the individual ability to metabolize a specific drug after administration of test dose. Phenotyping determines the actual metabolic capacities,
which may be influenced by any known or unknown covariates, including genetic as well as environmental factors\textsuperscript{10}.

It has been suggested that, genotyping/phenotyping of \textit{CYP2D6} enzyme activity can be applied by clinical laboratory for better therapeutic management\textsuperscript{11}. Though it has very well established in developed countries, it has not been initiated in any of the hospitals in the developing countries like India. Therefore, it is highly required to standardize the phenotyping technique in some of the premier hospitals like Jawaharlal Institute of Post-graduate Medical Education and Research, Pondicherry, where the present study was undertaken.