

## Review Article

# Flow Injection/Sequential Injection Analysis Systems: Potential Use as Tools for Rapid Liver Diseases Biomarker Study

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Flow injection/sequential injection analysis (FIA/SIA) systems are suitable for carrying out automatic wet chemical/biochemical reactions with reduced volume and time consumption. Various parts of the system such as pump, valve, and reactor may be built or adapted from available materials. Therefore the systems can be at lower cost as compared to other instrumentation-based analysis systems. Their applications for determination of biomarkers for liver diseases have been demonstrated in various formats of operation but only a few and limited types of biomarkers have been used as model analytes. This paper summarizes these applications for different types of reactions as a guide for using flow-based systems in more biomarker and/or multibiomarker studies.

## 1. Introduction

Liver diseases (hepatic diseases) cover the broad range of liver disorders. The liver has many important functions including breaking down toxic substances in the body and excreting them into urine, producing and secreting bile to aid in food digestion, converting glucose into stored glycogen and *vice versa*, metabolizing ingested medicines to obtain active ingredients, and producing blood-clotting factors, amino acids and cholesterol to transport fat. Damage to the liver will cause disruption of these functions which can cause serious damage to the body. Even though the liver is considered the only organ in the body that has exceptional capability in replacing damaged cells, if too many liver cells are damaged, the liver may fail to perform properly. Symptoms caused from liver failure may not be obvious until many liver cells (up to 75%) have malfunctioned [1]. Detection of liver problems at an early stage would increase the chances of curing them. Liver biopsy is currently the best method for diagnosis of chronic liver diseases [2, 3]. However, biopsy procedure involves the rather invasive method of taking a small piece of liver tissue to be examined under a microscope. The repetition of liver biopsy during diagnosis and treatment is hard on patients. Since liver diseases can also affect almost

all other body systems, many substances/chemicals in the body may respond to the malfunctioning of the liver. The use of these substances/chemicals as biomarkers has become an area of high interest in research as scientists look for alternative noninvasive diagnostic approaches [2, 4, 5]. Even though none of the biomarkers alone nor the liver biopsy is perfect, they can be used for indication whether further investigation is required [2].

Studies for the effectiveness of biomarkers involve the collection of numerous samples which may be available at different periods of time. Then the analyses of those samples are usually carried out using the same method for comparison. Most of the possible biomarkers being proposed and under study are biomolecules such as proteins and enzymes [6–9]. Analysis of biomarkers in samples with complicated matrices like body fluids requires highly specific and sensitive techniques. Immunoassay is one of the most widely used techniques for these purposes [10]. It can be used to quantify proteins, enzymes, and other biomolecules owing to the flexibility of the immunoassay format and the available antibodies. Fluorescence- and chemiluminescence-based techniques are also of interest due to their high sensitivity [11, 12]. However, these techniques are time consuming and require a skillful operator. From the many