

Research-based on Herbs Exploration and Use of Animal Models : Nature Materials Towards Supporting Evidence Based Medicine

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Abstract

Evidence based medicine (EBM) can be defined as clinical expertise informed by the best available evidence obtained from systematic research. However, definitions of both clinical expertise and best evidence remain a problem. The use of herbal-based traditional medicine is a legacy handed down from our ancestors and existence related to the culture of Indonesia. Some drugs are now used of herbal-based is derived from plants include, among others obtained by extraction or synthesis. Medicinal plant-based research in our laboratory indicate a pharmacological effect against some diseases, such as diabetes mellitus, hipercholesterolemia, rheumatoid arthritis, cancer and also antifertility. The results are still encouraging our team to continue to conduct exploration of bioactive substances from medicinal plants native Indonesia. Some bio-molecular analysis techniques have been conducted in our laboratory even in Brawijaya University already have equipment that capable for analyzing the molecular expression of proteins, enzymes and cytokines that were released and synthesized during the disease progresses. To support natural ingredients and herbal medicine toward evidence-based medicine (EBM), the research using experimental animals or cell cultures become necessary. This paper will explain briefly the results of plant-based traditional medicine research which empirically has proven capable of treating some diseases but need to be studied, but still need to do the research to answer the "why can heal?" and "how it works at the cellular and molecular level?" The results of this research opens a wider opportunity to develop further research is original.

Key words : Evidence Base Medicine (EBM), herbal medicine, bioactive

Introduction

The use of traditional medicine is a legacy handed down from our ancestors, and its presence related to the culture of Indonesia. Some drugs are now used was based on herb either single or ingredient is derived from plants include, obtained by extraction or synthesis process. Indonesia is one country "megadiversity" which is rich in biodiversity. Each species of plants, animals and micro-organisms have chemical values in producing a wide variety of chemical compounds.

In the history of drug development, the Indonesian nation has a lot of concocting potions and perform traditional treatment, which is also an important part of the discovery of several types of drugs. But on the other hand is often a concern for history is ignored, so much data that are not well documented, and findings that have even become international patent by the inventor is not the Indonesian people.

According to the definition of the Ministry of Health of the Republic of Indonesia, traditional medicine is defined as drugs or natural ingredients derived from plants, animals, minerals, and mixtures of these materials which have traditionally been used for treatment based on experience. But the reality of traditional medicines derived from plant portion is larger than that derived from animals or minerals, so the term for traditional medicine is almost always synonymous with medicinal plants because most of the traditional medicine raw materials derived from medicinal plants.

The development of science-based treatment plant origin bioactive.

The development of medical science-based bioactive has increased rapidly. More and more researchers who carried out exploration in bioactive medicinal plants to determine the content and the benefits for improving the quality of human life. Until now widely empirically proven medicinal plants in treating illness . The discovery of many medicinal plants showed a pharmacological effect on some diseases, such as diabetes mellitus, hipercholesterolemia, rheumatoid arthritis, liver dysfunction, cancer and antifertility also encouraged some researchers to explore the bioactive from medicinal plants. For the purposes of this pre-screening test to test in vitro and in vivo to determine the role of bioactive they contain. However, few studies have been done is not clear. In addition, the mechanisms of drug action is related to the patho very complex mechanism, also caused by the use of methods that are still macro, so that the biomolecular analysis technique is an option that should be done to support traditional medicine toward evidence-based medicine (EBM). For the purposes of this pre-screening test to test in vitro and in vivo to determine the role of bioactive they contain. However, few studies have been

done is not clear. In addition, the mechanisms of drug action is related to the patho very complex mechanism, also caused by the use of methods that are still macro, so that the biomolecular analysis technique is an option that should be done to support traditional medicine toward evidence-based medicine (EBM). EBM aims to apply the best available evidence gained from the scientific method to clinical decision making. So the use of research models in vitro, cell culture or experimental animals is one option, before applied to humans.

Several biomolecular analysis has been conducted in several research centers and universities, even in complex R & D Health Laboratory has been equipped advanced equipment capable of analyzing the molecular expression of proteins, enzymes and cytokines are released and synthesized during the disease process that began in progress and a character of a specific disease.

This paper will briefly describe the testing of plant-based traditional medicine which empirically has proven capable of treating some diseases but need to be studied, but still need to do the research to answer the "why can heal?" and "how it works at the cellular and molecular level?" The results of this research opens a wider opportunity to develop further research is original.

Our results explain how the content of the plant that serves as an antioxidant capable of improving the degree of type 1 diabetic rats insulinitis is prepared by providing exposure to Multi Low Dose streptozotocin (MLD-STZ) at a dose of 20 mg / KgBW. Streptozotocin (STZ) or name trivialnya 2-deoxy-2-(3 - (methyl-3-nitroureido)-D-glucopyranose) was synthesized by Streptomyces achromogenes and used to induce diabetes mellitus type 1 and type 2 diabetes mellitus (Pechhold et al., 2001; Szkudelski, 2001,). According to its group of origin, Streptozotocin is a nitrosourea that serves as an alkylation agent. STZ spontaneously decomposed to produce carbon ions of high reactivity with alkaline cellular components, including DNA and proteins. STZ damage the pancreatic beta cells in two ways: 1) alkylation of DNA through alkilnya group, and 2) as a NO donor that will increase the amount of NO in the pancreas. This excess NO reacts with superoksida to form peroxynitrite, which is very toxic to pancreatic beta cells (Szkudelski, 2001).

The mechanisms of diseases and bioactive action can be confirmed using immunohistochemical techniques, such as pancreatic beta cell apoptosis, as in

Figure 1. Using the TUNEL method can be definitely confirmed in pancreatic beta cells that had apoptotic nucleus of a visible color. Cells undergoing apoptosis essentially will look brown and fragmented DNA, by looking at differences in the core color with a small magnification can be distinguished and known to cells undergoing apoptosis. TUNEL method is specific for detecting apoptosis in each cell in the network with a label immunohistochemistry principles of DNA strand interruption.

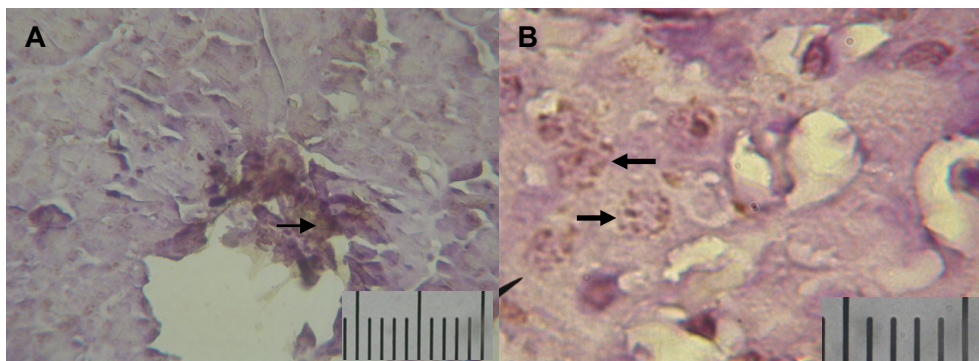


Figure 1. Apoptosis of pancreatic beta cells
(A:Apoptosis of pancreatic beta cells, B: Apoptosis of beta cells.
Black arrows indicate that apoptosis of pancreatic beta cells, 1 scale = 0.01 μm

During apoptosis of double-stranded DNA will be fragmented into single-stranded or oligonucleosome mononucleosom (nicks). This single strand can be identified using the label 3'OH terminal that has been modified nucleotide in enzymatic reactions (Lodish et al., 2000).

To study the benefit of other bioactive can also be learned through exposure to cell cultures that received antioxidants as cancer prevention and therapy based on enzyme function of protein kinase C- α . (Fig 2.). PKC enzyme involved in the process of proliferation and differentiation of smooth muscle cells. This event is controlled by a genetic mechanism as stimulation of extracellular signal-specific, ie, growth factor or mitogen. Path through which the signal transduction for cell proliferation is through activation of the race \rightarrow raf-1 \rightarrow MEK \rightarrow ERK \rightarrow transcriptional factor in the cell nucleus as shown in Figure 4.

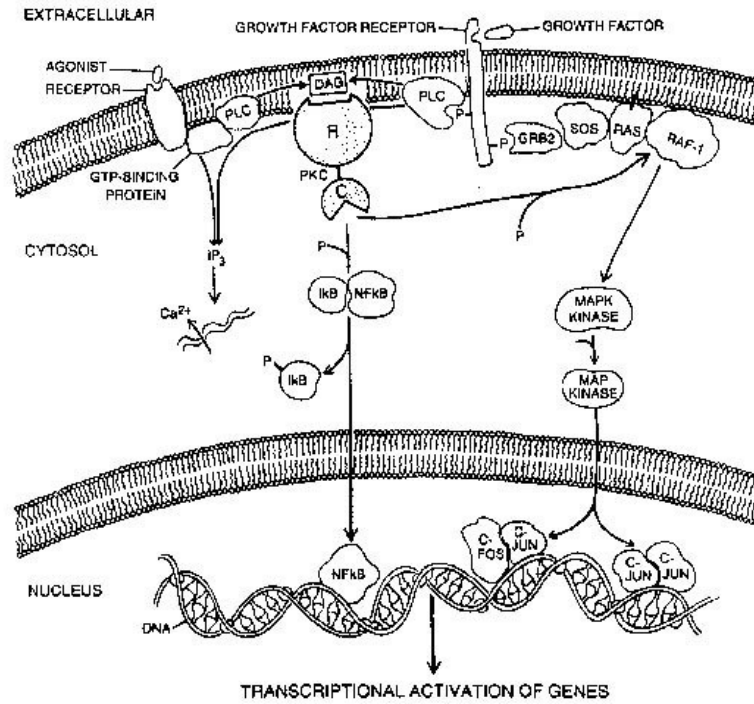


Figure 2.: The role of PKC enzyme in signal transduction in cell proliferation.

PKC enzyme activity and the expression used to observe the occurrence prolifersi and smooth muscle differentiation due to infectious agents as well as its treatment by the bioactive is contained in medicinal plants (Figure 3).

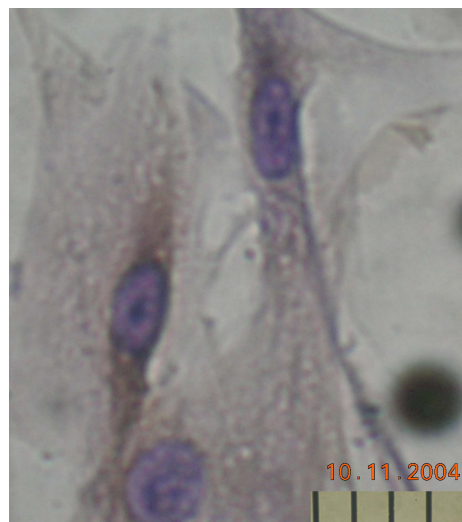


Figure 3: Expression of PKC- α isozyme in prostate smooth muscle cells dengan immunohistochemical techniques. (Aulanni'am &Purnomo, 2006) (brown color , indicated by blue arrows showed the expression of PKC- α isozyme present in the cytosol and perinuklear. 1 bar = 0.01 mm)

The role of plant-based traditional medicine for treatment can be studied as well as through the expression of protein from cell culture or experimental animals even at the level of use in humans by using electrophoresis (SDS-PAGE) (fig. 4). In addition to IHC (Immunohistochemistry) technique, SDS-PAGE still there are several ways that can be used, ie dot blot, Western blot and ELISA

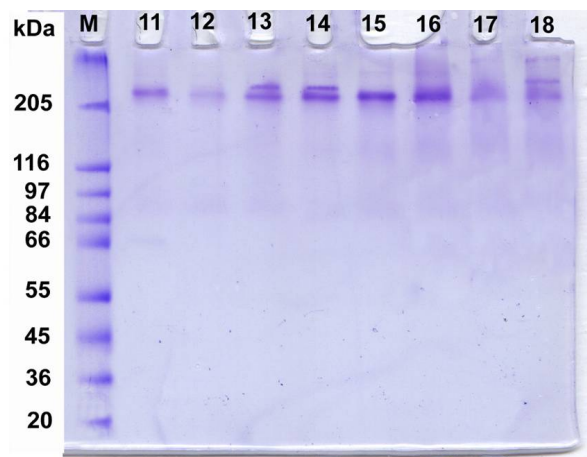


Figure 4. Erythrocyte Spectrin Membrane Protein Profiles of TF Patients who received Fe therapy

Conclusion

From the above description can be concluded Indonesian biodiversity of tropical plants that promise to be developed as a potential source of traditional medicine, but still need further studies on cellular and molecular level to explain the mechanism of action in inhibiting the occurrence of disease. Moreover, it can be used as the basis for the development of treatment efforts using the active ingredients of medicinal plants.

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