BAOJ Biotechnology

Jassem G Mahdi and Abigail J Manning, BAOJ Biotech 2016, 2: 1
2: 008

Case Report

Cross Molecular Recognition–An Approach for New Strategy for Drug Development

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Abstract

The association of medicinal plants and their therapeutic action is an interested subject which reflects the close relation of genomics and proteomics and DNA sequences among different biological systems. Since the early ancient era, human health and therapy has been supported by plants through the action of certain phyto chemical molecules. Some of these phyto chemical share their therapeutic action in both plants and human, including salicylic acid. In this respect, do humans and plants DNAs crosstalk to induce therapy through their molecular recognition between receptors and phyto chemical? If so, biotechnology and bioinformatics are significant potential techniques in the drug development.

Introduction

All living things share the same mode of biological activities through different cascade pathways. These pathways are fully controlled and managed by certain enzymes to maintain and regulate normal catabolism and anabolism in human and plants. The molecular composition of human and plant's genome and their expressed proteins reflect the similarity in both metabolism and biosynthesis. Therefore, both types of genomes have a similar role in over riding the dynamic biological process. Regardless the complexity of biological activities in human and plants, the molecular interactions between different molecules within or cross biological systems must consider molecular recognition concept.

Molecular recognition is a fundamental concept of how molecules communicate in harmony with their cohorts in complex microenvironments through non covalent bonding. Although a number of covalent drugs exhibit high potency, others exert toxic risks, due to the formation of reactive metabolites and idiosyncratic toxicities [1-4]. Nonetheless, understanding the genetic perspective of active phyto chemical biosynthesis and their corresponding pharmacological activities may contribute to a better strategy for designing safer and perhaps nontoxic drugs.

Various active photo chemicals are recognized by specific receptors in humans to initiate therapeutic changes. In this respect, inflammation is a group of gene-associated diseases which are caused by various extrinsic and intrinsic cellular molecular abnormalities. Defected gene(s) impacts on the expression of cellular proteins causing alteration of normal cell. The most common anti inflammatory drugs are aspirin, or acetylsalicylic acid, ibuprofen and naproxen (Figure 1). These drugs inhibit the biosynthesis of prostaglandins and thromboxanes, leading to anti-inflammation, analgesic and antipyretic effects. These drugs are classified as non steroidal anti-inflammatory drugs (NSAIDs). In plants, the precursor of acerylsalicylic acid (Figure 1), or salicylic acid (Figure 3) trigger different biological functions, mainly in plant's immune system when plants exposed to biotic (microbial) or abiotic (environmental) stresses [5-8]. It is interestingly, that using acetylsalicylic acid [1] induced therapeutic effects against tobacco mosaic virus in tobacco plant [9]. Furthermore, salicylic acid trigger thermal production in Arum lilies plants [10]. *Per se*, the anti-inflammatory activities of salicylic acid (Figure 3) may be genetically associated with its biological function in plants. Therefore, the aim of the current article is to raise a question whether humans and plants genome crosstalk to initiate therapy through the pharmacological activities of potent *phyto chemicals*.

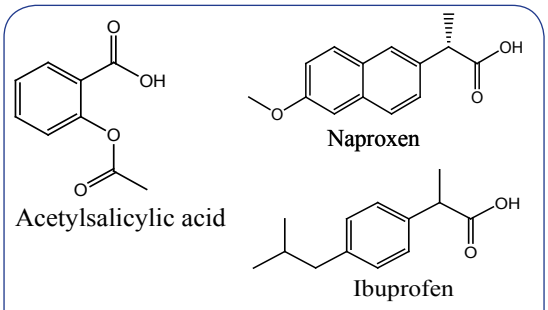

Figure 1: Chemical structure of common anti-inflammatory drugs

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Sub Date: February 26, 2016, **Acc Date:** March 10, 2016, **Pub Date:** March 11, 2016

Citation: Jassem G Mahdi and Abigail J Manning (2016) Cross Molecular Recognition–An Approach for New Strategy for Drug Development. BAOJ Biotech 2: 008.

Molecular Recognition

The intermolecular interaction between two molecules is often forming a complex molecule that can act as a prerequisite for induction of a biological function. This complex is characterized by thermodynamic and kinetic stability and selectivity, with optimum energy that allow exerting pharmacological function. In order to achieve effective level of recognition it is desirable that both molecules are in contact over a large area to establish the required non covalent bonding. In addition, the concept of molecular recognition helps understanding the mechanism of pharmacological process in terms of therapeutic or toxicity perspectives [11].

Molecular recognition involves two molecules to be compatible with each other in their structural conformations. The molecular recognition involves molecular interactions via a number of non covalent bonds such as hydrogen bonding, ionic, hydrophobic and Vander Waals interactions. These interactions not only maintain the dynamic recognition process between ligands and receptors in the biological system, but they are crucial for sustaining the conformational structure of macromolecules, including mainly proteins and nucleic acids. In living biological system specific photochemical molecules are recognized by their corresponding macromolecules causing the initiation of signaling, promotion and progression of blocking cascade pathways (Figure 2). This starts with signaling which is initiated through the molecular recognition of biologically active phyto molecules to fits binding site of the receptor, causing promotion of blocking of the interaction of the substrates with their corresponding enzyme cascade. An example for this concept is blocking the anadamide-degrading membrane enzymes fatty acid amide hydrolase by NSAID drug via promoting endocannabinoid signaling [12].

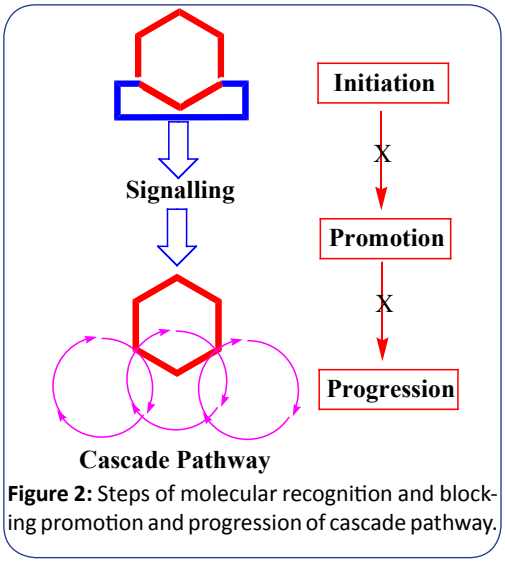

Figure 2: Steps of molecular recognition and blocking promotion and progression of cascade pathway.

Therefore, understanding the genetic and molecular recognition points of view may lead to better insight to the relationship between specific photo chemicals and their pharmacological action in human microenvironment. Furthermore, understanding of genetic setting may explain the manner in which how molecules interact with each other.

Phyto chemical and Macromolecule

In order to exploit the concept of molecular recognition in drug development, we may be considered a couple of simple phyto molecules, as examples. The most common simple phenolic drugs are salicylic acid (Figure 3) and its acetyl derivative, acetylsalicylic acid (Figure 1). These drugs can be recognized stero specifically by inflammatory proteins such as COX-2 and NF-κB [13-16]. This biocompatibility raises a question how the biosynthesis of a phyto molecule is set up to exert its therapeutic effect in different microenvironments. Is it coincidence or a result of a precise genetic engineering setting for some molecules to be recognized by different biological system? In addition, why does the human biological system preferentially utilize salicylic acid while β–D-salicin (Figure 3) must be converted to *salicyl* alcohol then to salicylic acid (Figure3) to exert it pharmacological function? Both salicylic acid and β–D-salicin (Figure 3) are good examples in this concept, as both *phyto chemicals* exert biological functions in humans and plants [17-21].

Owing to the random nature of macromolecules recognition to phyto molecules, this may generate an expression on how molecules communicate with each other to produce specific function. However, the random interaction may not be suitable in a complex dynamic biological system, and thus may result in errors. Therefore, it seems most likely that a genetic match may occur between specific phyto biosynthetic and therapeutic biological activities

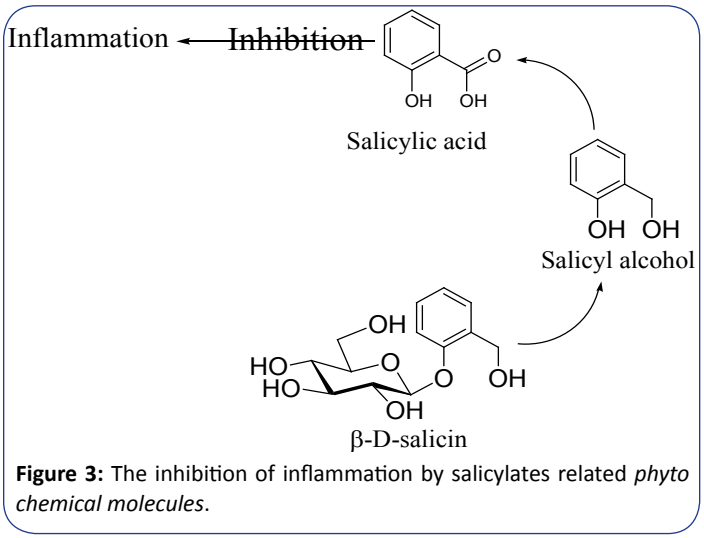

Figure 3: The inhibition of inflammation by salicylates related *phyto chemical molecules*.

to restore clinical problems. The diversity of herbal medication according to type of plant has been known since the Doctrine of Signatures [22], a philosophy that rationalizes the relation between how a plant looked, God's signature, and how it may be utilized to treat ill health [23]. In addition, the close proximity between plants and humans may encourage genetic co evolution that drives compatibility between the biosynthesis of phyto molecules and their pharmacological functions. In both cases, different ecological factors may contribute to the genetic setting at certain point since the creation of the earth. Meanwhile, the factors that cause infectious and noninfectious diseases are still present to this day. This means that the physiology of living things must follow the same rules of physiological compatibility. In addition, various plants synthesize both salicylic acid and β-D-salicin (Figure 3). The anti inflammatory benefit of willow, for example, has been well recognized since ancient civilizations [18]. The medicinal virtue of this tree encouraged the discovery of aspirin late 19th century.

The factors that contribute to health and disease often relate to a balance between the benefit of *phyto chemicals* and diseases. Therefore, physiological compatibility in living organisms is a crucial issue that depends upon a genetic engineering setting. Indeed the setting of genetic codes in biological systems is responsible for organizing and managing the entire biological activities. *Per se*, all physiological systems must be genetically engineered to be compatible within their ecosystem. There is huge number of medicinal plants, known or unknown, which have attracted innovation to exploit their pharmacological potential. *Phyto chemicals* and other natural products are evidence of various studies that lead to different hypotheses and theories, including doctrine and co evolution [24-26], that both based on the observations of their medical benefit.

If we consider genetic engineering to be the basis for physiological compatibility, harmony must occur between plant biosynthesis and pharmacological benefits of biologically active phyto chemical molecules. In general, all biological activities in living systems must be carried out via the activation/inhibition of certain proteins. In this respect, pollutants may induce inflammation that simultaneously triggers the synthesis of prostaglandin that can be inhibited by some natural products, such as salicylic acid. The synthesis of COX-2 may cross talk with the biosynthesis of salicylic acid in a way to complement the genetic engineering DNAs in humans and plants.

Despite the complexity of the structure of DNA, it is only comprised of four repeating nucleotide units; adenine, cytosine, guanine, and thymine. Therefore, the building blocks of DNA of humans and plants are structurally similar. However, all DNA structures of living systems vary in their sequence arrangement pattern of nucleotide units. In order to understand the relationship between biosynthesis and pharmacological properties of specific phyto molecule, it is important to consider the pattern of the encoded enzymes in biosynthetic and pharmacological pathways. The interaction of phyto molecule with an enzyme requires recognition of amino acid consensus motifs of the protein. In addition, the pattern of recognition must have its root in the encoded gene(s) that control both biosynthesis and pharmacology pathways. In this respect, the availability of high-throughput technologies in the genome and various databases are considered vital for a bioinformatics approach for the analysis of DNA sequence [27-30]. The genetic approach that encompasses an encoded specific gene and or the corresponding expressed proteins may aid the understanding of the complementary functional relationship of phyto secondary metabolites. This may encourage the development of a new biotechnological strategy for therapeutic intervention of certain clinical cases. Mapping of encoded - related genes and the analysis of nucleotides/amino acids sequences of cascade networks, bioinformatically can aid to facilitate an understanding into the pattern of the crosstalk between biosynthesis of a phyto molecule and its pharmacological potential. High-throughput serial analysis of gene expression and massively parallel signature sequencing allow for the study sequences and expressions of macromolecules.

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