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Decoding Epigenetic Mechanisms as Vital Tools for Maintaining Pharmacological Potency of Herbal Medicines

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Abstract

Studies have confirmed that heritable phenotypic variation in plants does not necessarily need to be based on the DNA sequence. Epigenetic studies have shown that the genomic DNA sequence might remain the same while gene expression changed by environmental conditions. This results in different morphologies and divers' chemical products from same species of a plant. Thus, in this paper we highlight that the herbal medicine industry should always be considering the habitat of a plant and its growing conditions as it does affect the pharmacological potency of the metabolites produced. The various aspects studied in this paper show that there is a need of optimizing the production sites of herbal medicinal plants because ecological factors influence epigenetic gene expression changes. This eventually affects the quality, quantity and efficacy of the secondary metabolites or drugs synthesized by the plants. Traditional herbalists have learnt this phenomenon by experience. Therefore, the value and exploitation of herbal medicine for modern human maladies shall greatly benefit by understanding the ecological influence of epigenetic mechanisms on medicinal potency.

Keywords: Metabolites; Plant Ecology; Chinese Medicine; Drugs; Metabolism; Climate Change

Introduction

Epigenetic regulations of the genome involve different chemical modifications at the molecular level that cause changes in gene expressions. These changes in gene expression can be inherited so as to ensure the survival of the species in future. Studies by Douma, et al. [1] showed that plants have strategies which enable them to mitigate short-term negative impacts in the environment without compromising future fitness. There are several known types of epigenetic mechanisms that organisms use to regulate gene expression in relation to the environment. These include cytosine DNA methylation, histone modification chromatin folding and RNA interference [2]. Broadly speaking, these mechanisms are being utilized by plants for defense against pathogens and for survival in case of other biotic and abiotic stresses. Some of the metabolites produced by plants under divers' conditions have been utilized by the herbal industry for treating many illnesses. Although there are studies on biotic interactions and their links to epigenetic and phenotypic variation, there is little study on the relationship between the environment and variations in the biochemical products produced due to epigenetic polymorphisms in plants [3]. This review focuses on this dimension and relates it to the quality and potency of the products in herbal medicine. Ecologist and molecular biologists have showed the effects

of growing plants in different locations as related to the secondary metabolites produced [4].

Plant Metabolism and the Formation of ECADS

Plants usually need water, carbon dioxide, minerals beside other abiotic factors like light and temperature to be able to grow properly. In natural conditions the earth presents plants with many conditions including biotic interactions with pollinators, fungi, herbivores and bacteria. The fitness of a plant in such situations is highly modulated by internal and external factors [5]. Hardly will a plant growing in nature have exact conditions as another plant even when it is growing ten meters away. Agricultural practices and mechanization have tried to make more uniform conditions for plants to grow in similar conditions. These practices enable plants to growth and have more or less similar heights, growth rates, and yields resulting in more economic gains. However, naturally, plants tend to adjust to environmental stresses by regulating the number of genes expressed at a particular environmental condition using epigenetic mechanisms. When a particular set of genes are expressed and the plant survives and produces seeds, the plant keeps a memory of the genes expressed. This is called an epigenetic memory. It is amongst the first steps towards speciation. Some plant species have adjusted these changes in gene expression so much such that the physical appearances are absolutely different. This can make one think that they plants are two different species. Studies in biosystematics have identified differences in morphology, cytogenetics, biochemical and physiology which are not observed at the genetic level. This has led to a group of plants called ecads. For example, *Euphorbia hirta*, grows in prostrate forms in disturbed area but becomes erect in undisturbed area. However, biosystematic studies in experimental field show that these morphological variations are not genetically fixed but are regulated by the environment as the plants become erect in better habitats.

Epigenetics and the Economics of Crops

Abiotic stresses have also influenced marketing of crops. Some fruits of the same species grown in particular locations have been found to be sweeter and tastier compared to others grown in different places. For example, oranges and bananas from Africa are sweeter than those grown in temperate zones. This sweetness is as a result of hotter environmental conditions and the presence of less water conditions. Epigenetic studies show more sweet genes are expressed than in colder areas in which the plants perceive as adverse conditions. The reverse is also true for apples grown in temperate zones. The apples from temperate zones are sweeter than those grown on tropical conditions. The influence of the surroundings of a plant have been known to have profound effects on the plant metabolism and metabolites. For example, a gaseous plant hormone called ethylene was found to regulate numerous plant and fruit biological processes like ripening to even developmental responses [6].

Epigenetics and the Herbal Medicine Industry

In all living organisms, it has been shown that the products of metabolism are as a result of translated genes. The central dogma of molecular biology shows the unidirectional flow of information from the DNA to RNA and later into translated products. However, this flow has been shown to be influenced by the environmental conditions. Hence, the observed phenotype is a result of the genetic plus environment and their interactions thereof:

Phenotype = genetic constitution + Environmental pressure + interactions outcomes

Thus phenotype is not only the external or morphology of the plant but also the size, number and structure of cells, number, size and structure of chromosomes, the biochemical composition of metabolites and the rate and magnitude of plant physiological processes taking place. The biochemical expression of the plant gives it its unique characteristics which are utilized by the herbal medicine industry.

Epigenetics, Pathogens and Climate Change

Microbes are ubiquitous. They depend and interact with other organisms to survive. They normally seek sources of energy from divers' places. Plants like animals have ways of detecting and inhibiting the attacks of microbes. Some plants produce chemicals which destroy or deter microbial metabolic functions. Some microbes are also aggressive and can devise ways of overcoming such defense mechanisms. This is one of the reasons for outbreak of new diseases. Plants have to be healthy in order also to adjust and defend themselves from such onslaughts.

Plants utilize an epigenetic approach to resist fungal, bacterial and others biotic stresses, however, microbes also have been found to employ epigenetic mechanisms to

modulate their growth and pathogenicity. This leads to microbial resistance against the plant immunity [7]. Climate changes can increase the stresses of both plants and microbes in equal measure, but microbes have a faster way of adjusting to stresses compared to plants. There is need to study such biotic-induced epigenetic changes on specific gene loci and thereafter link them to specific plant molecular signaling genes in the future [3]. It is interesting to note that the same mechanism takes place in animals and human beings but a faster rate. The causes of cancer and other lifestyle related disorders are caused by human beings altering the external and internal environments which cells and metabolic reactions are supposed to be taking place. These changes in the environment have been confirmed to affect plant growth and the metabolites thereof, for example the use of herbicides showed differential responses of different crop cultivars to the same herbicide however, recommendations by companies of herbicide use is mainly crop-specific although sensitivity and response of crop cultivars can be different to herbicides [8,9]. Other studies have shown that habitat altitude, annual sun shine, temperatures can influence the active substance contents and their antioxidant activity and hence they can be used in selecting sites for drug production in the herbal medicine industry. For example, For example, altitude and temperature significantly and positively correlated to the contents of chlorogenic acid and flavonoids ($P < 0.05$) in *Eucommia ulmoides* Oliv. [4].

The Need for Herbal Medicine to Embrace Epigenetic for Pharmacological Potency

Herbal medicine relies on specific chemical metabolites produced by plants to produce effective drugs. The specificity of these chemical has largely been based on identifying the right plant species. However epigenetic studies show that the products of metabolisms are highly influenced by the environment [10]. This explains why it is important to consider the habitat where a particular medicinal plant was grown (Figure 1).

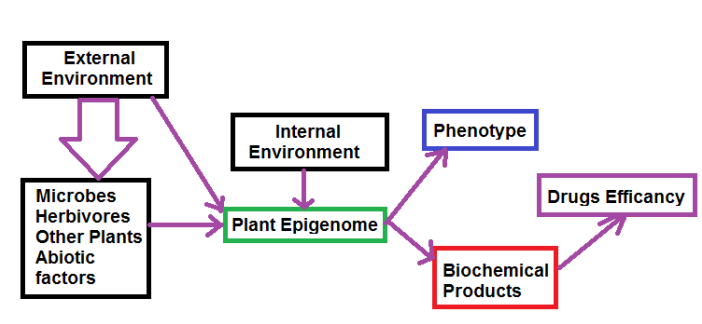

Figure 1: The relationship between environment, the plant epigenome and the quality and efficacy of drugs produced for medicinal purposes. Epigenetic studies show that gene expression is highly influenced by the environment.

Other studies have shown that plant epigenetic variations contribute to variations in plant phenotypic traits as observed in natural populations [11]. Furthermore, it has been shown that these epigenetic variations reside at transposable elements or their residuals. The environmental pressures in this transposable element loci where shown to influence gene expression and hence phenotypic variations, this makes us to conclude that biochemical products produced are also varied and hence implies that they have differences in drug efficacy when administered [12]. Studies by Peñuelas and Llusià [13], showed that certain plant metabolites are actually only synthesized under specific environmental conditions and their contents significantly increased under specific environmental conditions.

Experiences of Herbalists in Africa

Traditional herbalists have learnt by experience that medicinal plants are quality and efficacy differentiated by locations. We have had herbalist who know of particular trees which have healing properties. These herbalists do not consider all the other species but only species from particular places. This can now be explained epigenetically. It is on these other places where we can find stress levels that are conducive for the production of the active lead compounds of the drugs. It has also observed that they also collect the leafy plant materials only at the early hours of the morning. This is the time when there is less photosynthesis is taking place and the starch produced in the previous day has already been converted to essential

compounds unique to the species. How we can now explain this accumulated medically effective traditional protocol is absolutely phenomenal. These experiences have also been observed in China, whereby only *Panax ginseng* CA Mey, produced in the northeastern part of China is the only one officially recognized as a medicinal drug [14].

Conclusions and Further Studies

The above studies show that epigenetic mechanisms are influenced by environmental conditions and are capable of either switching off a gene activity or fine tuning an existing gene activity for plant survival. We therefore, suggest that further research be done by combining ecologists, health molecular biologists and genomic experts on various medicinal plants in different environmental conditions to determine other variations in drug components which could also be triggering allergies in some people but not in others. For example, a greenhouse grown onion (*Allium cepa*) can be allergic to somebody but an open space grown onion can be of no effect to the immune system of the same person. This is because a plant which is adapting to a different environment can have phenotypic plasticity and biochemical products differences. These revelations can be used in experimental field studies and genomics to grow herbal species with an aim of increasing the quality, quantity and efficacy of drugs.

Declarations

I declare to conflict of interest

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