

Public Abstract

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Title:Curcumin regulates transcription in *Dictyostelium discoideum*

Botanicals are widely used as dietary supplements and for the prevention and treatment of a myriad of diseases ranging from the common cold to depression. One in four Americans uses a botanical as part of their primary healthcare with billions of dollars spent annually. Curcumin, the active ingredient in turmeric, has gained a lot attention in recent years for its therapeutic uses and has been linked to a wide spectrum of pharmacological effects including anti-carcinogenic, anti-inflammatory, Alzheimer's prevention and antioxidant activity. Despite the large and growing interest in the use of botanicals such as curcumin in disease treatment and prevention, there is little evidence regarding their efficacy, safety and long-term effects. Importantly, the fundamental mechanisms associated with the cellular response to botanicals are generally not clearly understood, and there are often unknown off-target effects. This is supported by the bafflingly large number of effects associated with curcumin.

The use of suitable model systems in pharmacogenetic analysis allows for the subsequent characterization of genes and their protein products to explain the mechanisms of drug action. Understanding the complex mechanisms associated with drug response is compounded by the use of mammalian models. In addition, the maintenance and care of such models, the large numbers of animals required for experimental study as well as ethical concerns have necessitated the use of simple and genetically tractable non-mammalian models.

The social amoeba, *Dictyostelium discoideum*, has proven to be an excellent model for the molecular and genetic study of the mechanisms of action of drugs and their effects on the cell. *D. discoideum* has been successfully used to find targets to improve efficacy of drugs used in psychiatry and cancer treatment. Those studies were subsequently validated in human cells.

By taking advantage of this simple but powerful biological model and the molecular genetic tools available to us, we have started to investigate the complex effects of the botanical compound curcumin on cell growth, cell physiology and the underlying molecular mechanisms of action. Results from our studies revealed a rather complex pleiotropic response to curcumin including effects on proliferation, oxidative stress and a global regulation of gene expression at the transcriptional level.

The relative lack of conclusive scientific evidence regarding the therapeutic benefits of curcumin, coupled with curcumin's possible deleterious effects as revealed by our research findings, underscore the importance of further research to establish curcumin's risks and benefits. Ascertaining the risk-benefits of curcumin with more conclusive scientific evidence would better equip consumers to make decisions about using curcumin, and in fact other botanicals, as part of their primary healthcare.