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Importance of DNA Microarray in Herbal Drug Technology



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ABSTRACT

The details on the DNA microarray approach are provided in this review paper. One of the molecular detection methods is the DNA microarray, which consists of a collection of microscopic features (often DNA) attached to a solid surface. DNA is connected to solid supports called DNA microarrays in the prearranged organized grid pattern. These supports are typically constructed of silicon or glass. With the use of hybridization and subsequent detection of the hybridization events, microarrays, a technology in which thousands of nucleic acids are attached to the surface, can be used to determine the relative concentration of nucleic acids of sequences in the mixture. Applications of natural products in medication development and discovery are growing. They can influence multiple targets at once in a complex system due to their diversity in chemical composition. It becomes vital to analyze gene expression in order to comprehend molecular mechanisms better. Traditional expression profiling methods are designed for single gene analyses. DNA microarrays are an effective high-throughput method for analyzing numerous genes at once. DNA polymorphism and mutation analysis continues to be the principal practical application of DNA microarrays. This study focuses on the significance of DNA microarrays, their methods, conditions, and applications in pharmacodynamics, pharmacognosy - the assessment of the efficacy of herbal remedies and extracts and pharmacogenomics.



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INTRODUCTION:

“DNA microarray” is also termed as DNA chips, gene chips, DNA arrays, gene arrays and biochips. Biochips are the most recent generation of DNA probe-based biosensors. Understanding gene functions is a significant post-genomics task. To assign the role of genes in molecular networks, methods such as proteomics, transcriptomics and metabolomics are used. A cell’s gene expression profile dictates its phenotypic function, and responsiveness to its environment. A cell’s complement of genes is very dynamic and responds quickly to environmental stimuli. As a result, gene expression analysis is required to provide information concerning regulatory mechanisms, metabolic pathways, and broader cellular function. Because thousands of genes and their products work in a complex and coordinated manner in any live thing technologies with a high degree of automation are required for genome-wide expression analysis. DNA microarrays were created in response to the requirement for a high-throughput, efficient, and comprehensive technique that can investigate all or a substantially specified fraction of the genes encoded by a genome at the same time (1, 2). In research, microarrays are used in conjunction with other techniques such as differential display PCR, northern blots (3), quantitative PCR, serial analysis of gene expression (SAGE) (4,5), and TIGR orthologous gene alignments (TOGA) (6,7). Microarray applications quickly evolved to encompass the whole drug development process, with an initial concentration in the post-genomic age on detecting changes in gene expression for target identification. Pipeline (8–10). DNA microarrays are being used to study the transcriptional profile in a variety of physiological and pathological scenarios, which is leading to the discovery of new genes and molecular markers for the diagnosis, prediction, or prognosis of those conditions (11, 12). The success of DNA microarrays has led to the development of protein arrays advancement (13-15). Protein microarrays are primarily used to study protein function, screen antibodies (16) and recombinant proteins (17), discover proteins implicated in disease or potential drug targets, detect or diagnose disease quickly (18, 19), and screen for protein-protein, DNA-protein, and enzyme-protein substrate interactions (20, 21). The scarcity of full-length human gene clones, as well as the various idiosyncrasies of proteins in terms of stability and structure, impede high-density human protein arrays (22); Although protein microarrays have not yet reached the maturity level of DNA microarrays, recent discoveries have indicated that many of the technology’s limitations can be addressed (23, 24). Cell-based arrays, which use matrices of living cells designed to produce specific proteins, have recently emerged as useful methods for high-

throughput gene function investigation. These arrays can help with genome-scale research on several aspects of protein function, such as biochemical activities, gene disruption phenotypes, and protein-protein interactions (25, 26). A transfection microarray has been established as an alternative to protein microarrays for therapeutic target identification and as an expression cloning system for the finding of gene products that modify cellular physiology (27). To assist large-scale, high-throughput functional genomics research utilizing RNAi, a siRNA-transfected cell microarray has been constructed (28). Chemical microarrays, or arrays of tiny organic compounds, are a unique way to analyse chemical libraries. They are commonly utilised in miniaturized and high-throughput analyses of protein interactions with chemical molecules (29, 30). Several modified technologies, ranging from macromolecular microarrays to cell arrays, have opened up new avenues of research in molecular and physiological systems. The information is collected from article Scopus, pub med, science direct article.

DNA MICROARRAY

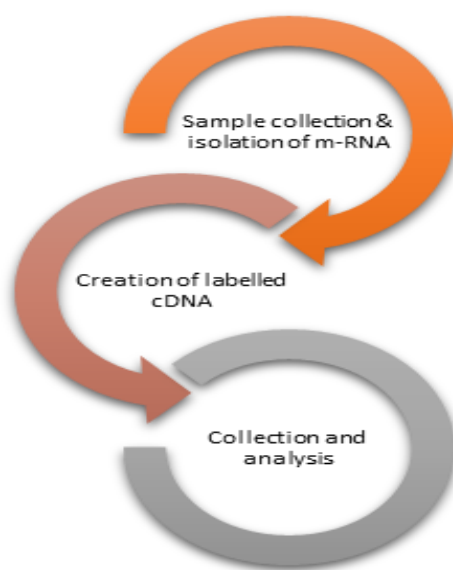


Fig No 01 Steps involved in DNA microarray

Thousands of oligonucleotides or identifiable sequenced genes are printed on a solid support that is impermeable to DNA, typically glass, silicon chips, or a nylon membrane, to create a DNA microarray. The devices are frequently referred to by terminology such as DNA arrays, gene chips, and biochips. The DNA microarray field is a conglomeration of technologies such as automated DNA sequencing, PCR-amplification of DNA, oligonucleotide synthesis, nucleic acid labeling chemicals, and bioinformatics. The two types of DNA microarrays that

are most frequently used are those where, Using photolithographic or other methods, the DNA is synthesized in-situ. These methods also include those in which the DNA (usually in the form of a cDNA or full-length ORF) is post-synthetically bonded to a solid support.(31, 32). DNA microarrays are employed for a variety of purposes, depending on the type of probe (immobilized DNA) used to construct the array and, ultimately, the information derived from (33, 34). In the context of microarrays, a ‘probe’ is the (partial)genomic sequence of a gene that has been deposited and placed on the microarray, whereas the ‘target’ is the biological sample material. Although there are many different protocols and types of microarray experiments, all of them involve isolating RNA or mRNA from suitable biological samples, applying a fluorescent tag to the RNA or cDNA copy of it, hybridizing the labelled RNA or cDNA to a microarray (probe) for a period of time before the excess is washed off, scanning the microarray under laser light, and data analysis with the proper software. Table 1 provides a brief summary of three fundamental types of DNA microarray investigations and their applications (35).

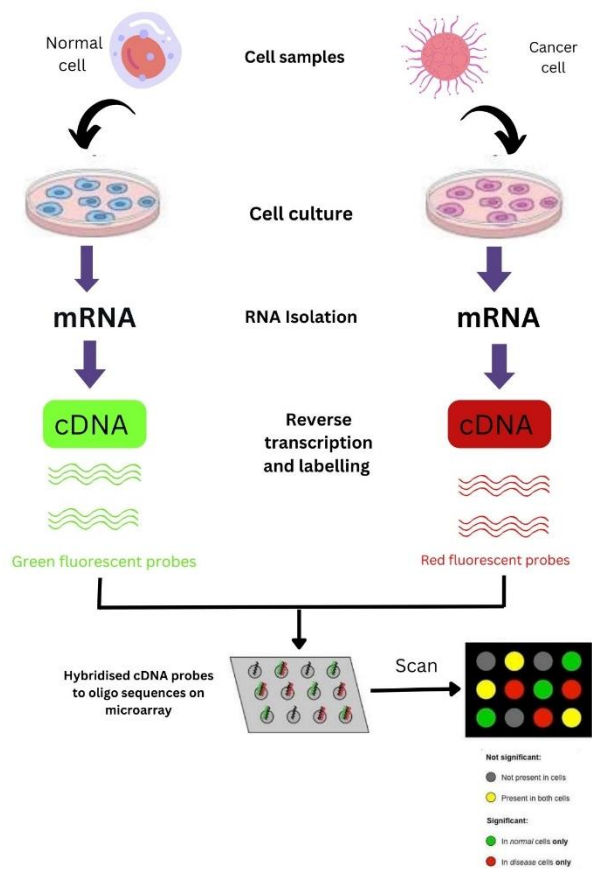


Fig No 02 Procedure of DNA microarray

1. APPLICATIONS

Many modern pharmaceuticals were first used in indigenous communities, and ethnobotanical data is frequently the foundation of study on natural products (56). A better understanding of the pharmacological effects of many medicinal plants traditionally used in medicine is one of the goals of ethnopharmaceutical research (57). Due to their greater structural variety when compared to conventional synthetic chemistry, plants are viewed as a possible source of new medicinal medicines. Plants can be used as a source of bioactive molecules that could be used to make medicines, which is a therapeutic agent. A natural product-based medication can be made in three different ways.

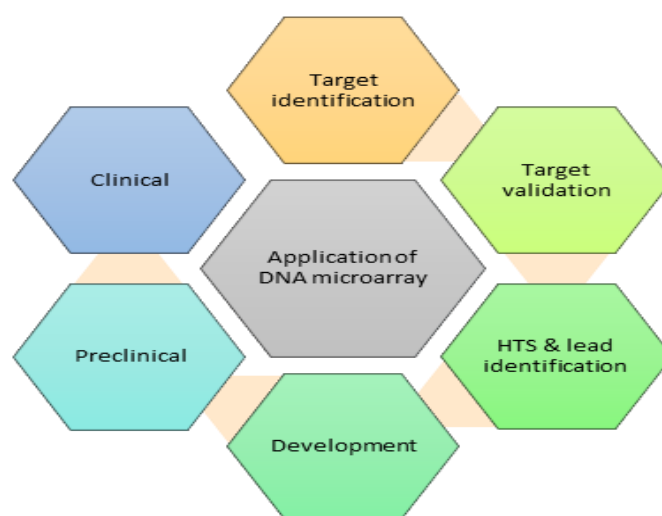


Fig No 03 Applications of DNA microarray

1. Pharmacodynamics employing DNA microarrays.

Herbal products are often whole herbs, with a variety of bioactive chemicals present in their formulations or extracts. A greater knowledge of the molecular mechanisms behind their biological activity is required due to the rising demand for herbal products that have been scientifically confirmed and standardized. Even though many herbal medicines' physiological effects are being investigated at the molecular level, it is still unknown what the targets of the various phytochemical components of herbs are and how these molecules contribute to biological activities.

2. Compounds Purified /specific phytochemical group

When examined with gene microarrays, the molecular mechanisms underlying the various biological activities of the triterpenoid compounds isolated from the tropical medicinal plant

Centella Asiatica revealed that these compounds cause a gene-expression response consistent with their common medical uses in the treatment of connective tissue disorders like microangiopathy and wound healing. The discovery of genes that are affected by these substances lays the groundwork for a molecular understanding of Centella's bioactivity and opens up possibilities for the quantitative correlation of this activity with clinical efficacy at a molecular level (34). The antiproliferative effects of the medicinal herb *Coptidis rhizoma* and its primary constituent, berberine, were also studied in human pancreatic cancer cell lines. Oligonucleotide arrays containing roughly 11,000 genes each were used to analyse the patterns of gene expression linked to each agent's sensitivities. Purified berberine and *C. rhizoma* both exhibited anti-proliferative properties, and both common and unique genes were shown to be involved (35). Using cDNA microarrays with 3000 human genes obtained from a leukocyte cDNA library, it was possible to analyse the role of genes in the apoptosis-inducing action of alkaloids from the root of the Chinese medicinal plant *Tripterygium hypoglaucom (levl.) Hutch (Celastraceae)*. *Tripterygium hypoglaucom* alkaloids have been shown to induce apoptosis through the c-myc and NF-kappa B signaling pathways (36). The inferior colliculus of DBA/2J mice experiencing audiogenic seizures and mice receiving Qingyangshenylycosides, a traditional Chinese medicine, were studied for gene expression patterns. A total of 134 genes were either up- or down-regulated during an audiogenic seizure, according to a gene expression investigation employing Agilent oligo microarray technology. Many of the gene expression changes brought on by audiogenic seizures were stopped by qingyangshenylycosides. However, the use of Qingyangshenylycosides resulted in the further enhancement or reversal of certain of the audiogenic seizure-induced genes. Important information on the molecular mechanisms of audiogenic seizures and the mechanism of action of Qingyangshenylycosides was supplied by the data (37). Using a DNA microarray technology, the mechanism of herbal glycoside recipes regaining impaired spatial learning memory in mice with cerebral ischemia/reperfusion was investigated. The groups with improved spatial learning abilities had their gene expression patterns examined. Numerous genes involved in controlling the cell cycle, signal transduction, nervous system transcription factors, DNA-binding proteins, etc., showed an increase in expression of 1.8-fold. In this investigation, nine genes were discovered that were connected to the retrieval of spatial learning memory deficits when treated with glycoside formulations (38).

3. Pharmacogenomics Employing DNA Microarrays

The study of genes and the gene products (proteins) necessary for pharmacological or toxicological reactions to medicinal substances is known as pharmacogenomics. To determine whether genes are activated or suppressed by xenobiotics, gene expression patterns can be examined using oligonucleotide-based DNA chip technology or cDNA microarrays (39). The development of a microarray genotyping system for multiplex analysis of a panel of single nucleotide polymorphisms (SNPs) in genes encoding proteins involved in blood pressure regulation has been attempted (40-42). This system will be used in a pilot study to show its viability in the pharmacogenetics of anti-hypertensive drug response. The use of DNA microarray technology may allow for the accurate prediction of a person's reaction (or lack thereof) to herbal medications. Many fields of biology, including toxicology, are now being impacted by technologies created to characterize genes and their products on a discovery scale. The branch of toxicology that combines genomes and toxicology is known as toxicogenomics. By comparing the results of an experimental chemical with a database, gene expression profiling enhances 4 mechanism-based research on toxicant action in toxicology. Microarray analysis has recently been shown to be useful for examining the impact of xenobiotics across the genome and for quickly identifying hazardous risks for novel medication candidates (43,44). ToxBlot II, a bespoke microarray with cDNAs representing 12564 human genes chosen for their possible relevance to a wide spectrum of toxicities, is an illustration of such a platform. In numerous cell lines tested, the results revealed up-regulation of IL-6 expression and down-regulation of PDGFR, APP-1, and KGF-1 expression. The frequent epithelial atrophy seen in chronic areca chewers in vivo may partially be explained by the down-regulation of KGF-1 expression in oral fibroblast cell lines, which may inhibit the proliferation of underlying keratinocytes. The areca nut extract toxicogenomic database was created by this study (46). The mRNA expression patterns of 1177 genes were also examined using cDNA microarray analysis in ten oral cancer patients who had a history of consuming betel nuts. To better understand the pathophysiology of oral cancer in nations like Taiwan where betel quid chewing is common, this study offers preliminary evidence (47).

4. Pharmacognosy Employing DNA Microarray

The first step in ensuring the quality, safety, and effectiveness of herbal medicines is the use of genuine herbal ingredients. Assays based on DNA polymorphism have been developed to

identify herbal medications (48,49). This method uses the polymerase chain reaction to amplify small amounts of DNA, and then the reaction products are examined via gel electrophoresis, sequencing, or hybridization using species-specific probes. Microarrays have recently been used to identify medicinal plants based on DNA sequences (50,51). Finding a distinctive DNA sequence that is particular to each species of medicinal plant is important in order to use DNA microarrays for the identification and verification of herbal material. The matching probe is then created on a silicon-based gene chip using the knowledge of the DNA sequence. If the test material being examined has complementary target DNA sequences, these probes can find them. Multiple poisonous traditional Chinese medicinal plant species can be identified by parallel genotyping utilizing a silicon-based DNA microarray that uses species-specific oligonucleotide probes (52). A cost-effective, accurate approach for quality control and safety monitoring of herbal medicines and nutraceuticals may be chip-based authentication of medicinal plants. It is challenging to identify herbal products since they frequently consist of dried or processed portions. This is especially true for botanical products that have a similar appearance but may have very different therapeutic qualities and market prices. The quality control and safety monitoring of herbal medicines and nutraceuticals may benefit from chip-based authentication of five medicinal plants, which will also greatly increase the therapeutic potential and financial viability of herbal products. This use of DNA microarrays will not only be advantageous to the herbal medicinal sector, but it may also make it easier for regulatory authorities to identify herbal goods. The molecular mechanisms and networks underlying the complex pharmacological activity of herbal extracts and mixes can be clarified using microarray analysis of gene expression. From a contemporary genetic perspective, studying the patterns of gene expression at various stages of the therapeutic process can reveal mechanisms and aid in the identification of biomarkers of an unfavourable or favourable response. A positive association between the transcriptional response elicited by a herbal medication and a database profile of an existing medicinal agent can help with a target specificity and mechanism of action investigation of the pathways downstream of the target. Additionally, it will aid in the discovery of brand-new medicinal uses for herbal medicines. Additionally, activity-guided fractionation of herbal extracts using DNA microarrays can help to identify the specific active ingredient responsible for the desired effect. Microarrays are used throughout the whole drug development process to enhance the choice of biological targets and lead compounds. The selection of the best candidate for medication development will be facilitated by the correlation of gene expression data of herbal medicine candidates with clinical outcomes or biomarkers of response in biological

systems. DNA microarrays will make it easier to produce individually optimized medications based on varied gene expression patterns in the field of pharmacogenomics. Studies on genetic polymorphism can be used to categorize people based on how well they can metabolize drugs or how they react to illness (53). High throughput, rapid evidence-based herbal medicine discovery via the Reverse Pharmacology method can be facilitated by microarray-based approach. A technology platform for the characterization of herbal compositions called Phytomics, which was recently developed and patented, uses Herbal Bio Response Arrays (HBR Arrays) to detect the bioactive components and biological activities of a herbal composition. (54)

DNA microarrays may be used at many stages of the development and discovery of herbal drugs. This entails quality assurance and standardisation of herbal medicines, the discovery of diagnostic, prognostic, and pharmacodynamic biomarkers, the identification and validation of new targets, the profiling of on-target and off-target effects during the optimisation of new therapeutic agents, and understanding molecular mechanisms of action and structure-activity.

Drug discovered by using DNA microarray Technique: (111)

Types of application	Drug tested	Disease
Target identification of drug	Traditional Chinese medicine (Trachelospermum Jasminoides)	Chronic degenerative joint disease
Molecular docking and simulation studies	Mitoxantrone, Leucovorin, Birinapant and Dynasore	SARS-CoV-2 M pro
Screening drug virtually	Rearranging Dequalinium	Allosteric modulation of hM2
Drug metabolism prediction	Drugs related to P450 cytochrome enzyme	Seniors' metabolism of medications and avoiding adverse drug events
Drug screening/discovery	All drugs correlated to viral proteins	SARS-CoV-2
Molecular docking and drug resistance	carbapenems	Enzyme of class OXA (Acinetobacte-r baumannii)
Molecular docking, molecular dynamic simulation	Approve drug libraries for ACE2	SARS-CoV-2
In silicon screening	Glycoprotein inhibitor	SARS-CoV-2
Drug rearranging	Medications that aim to regulate gene activity in pathway to address symptoms of depression	Resistant depression treatment
Pharmacological analysis	Jiani Pi Fu Recipe	Colon cancer LoVo cells metastasis

Construction of multi regulatory pathways	pancreatic cancer (pivotal drugs)	Pancreatic cancer
Drug repurposing		Hypertension
Pharmacological drug mechanism	Aloperine	CVS disease
Drug screening	Drugs targeting immune-related genes	Cervical cancer

5. CONCLUSION:

Microarray gene expression research can assist in elucidating the molecular mechanisms and networks underlying the complex pharmacological activity of herbal extracts and combinations.

Studying gene expression patterns at various stages of treatment can reveal mechanisms from a modern genetic perspective and aid in the identification of biomarkers of adverse or favorable responses. It will also aid in the discovery of new therapeutic applications for herbal drugs. In order to identify the active ingredient in herbal extracts that is responsible for the desired effect, DNA microarrays can also be employed for activity-guided fractionation of the extracts. To enhance the choice of biological targets and lead compounds, microarrays are employed throughout the drug discovery process. Gene expression data for potential herbal drugs and clinical results are correlated.

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