WHITE PAPER

The Future of Medicine:
Plant-inspired, Minimum Essential Mixtures

GbSciences

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As the digital world evolves, so does the potential for Artificial Intelligence (AI) to re-invent medicine as we know it. Using AI-enabled models of the human body, the paradigms that guide the development of new medicines can be changed to predict the outcomes of combination medications designed to address complex diseases and to minimize their corresponding side effects. A study by the Georgetown University Health Policy Institute estimates that more than 131 million Americans rely on at least one prescription medication, with that number increasing as people age. Data further suggests that greater than 50% of Americans take four medications daily on average.

What if a single formulation were available for patients that addressed their overall healthcare needs? Over time, the use of AI and Machine Learning (ML) tools will help create personalized medical solutions for individual patients. Right now, these tools can create more effective drugs for patients with specific diseases or disorders, but the digital era should provide new and better tools to create the personalized medicines that we all need to address our comprehensive medical requirements.

Plant-based remedies have been used for millennia as a part of Traditional Medicine Systems (TMS). TMS treatments are based on multiple active ingredients working in conjunction to address the many symptoms of complex human diseases. Technological innovations in AI, such as Machine Learning (ML), can now be used to create novel plant-inspired solutions based on TMS therapies. These novel plant-inspired medicines are designed to target the many contributing causes of neurodegenerative disease and other serious chronic illnesses.

Minimum Essential Mixtures:

Viable Alternatives to Single Ingredient Drugs

Current pharmaceuticals are developed to address a singular “cause” of a disease, and they do not provide a comprehensive and holistic approach to complex diseases. However, most human disorders are complex, and do not have a single cause. In a recent interview, President & CSO of Gb Sciences, Inc., Dr. Andrea Small-Howard, noted that individuals who take multiple medications are often prescribed one drug for the main “cause” of their ailments and several others to address the side effects caused by the primary medication. Dr. Small-Howard also pointed out that traditional medicines in the form of plant-based treatments are often overlooked as effective treatment options in the United States, but many cultures and countries back their efficacy.

Gb Science’s novel approach to translating TMS for Western medical systems is through Minimum Essential Mixtures (MEMs). MEMs contain different ingredients that are optimized to work together to treat the targeted disease. To create effective MEMs, Gb Sciences simplifies whole plant medications, which are composed of hundreds of active ingredients, into MEMs containing three to five bioactive compounds that demonstrate therapeutic synergy. Therapeutic synergy is achieved when the MEMs bioactivity is greater than the sum of each singular ingredient’s bioactivity. MEMs preserve the therapeutic synergies of whole plant medicines, but they are easier to manufacture with precision at scale, which makes MEMs a viable alternative to the standard approach of single ingredient drugs.

Gb Sciences' MEM-based drug development strategy does not aim to treat complex diseases as if they were caused by a single cause, but instead addresses the combination of factors that lead to a complex human disorder. MEMs are potentially more effective than single ingredient drugs because the different active ingredients target the multiple human processes responsible for complex diseases, such as neurodegeneration, heart disease, and cancers. As such, MEMs offer a more holistic treatment for complex disorders such as Parkinson's disease that cannot be attributed to a single cause, while maintaining the manufacturing and quality control advantages of single ingredient drugs.

Currently, several of Gb Sciences' MEM formulations have completed the critical preclinical proof-of-concept stage including novel plant-inspired MEMs for Parkinson's disease, chronic pain, inflammation, heart disease, and anxiety. Gb Sciences is moving these MEMs forward towards human clinical trials. Along with the benefit of treating complex diseases comprehensively, MEMs may lead to the personalization of medicine, which is a predicted future version of medicine where specific formulations may be created to serve the unique needs of individuals.

Using the Latest Technology to Advance Drug Formulations

The medications currently available at the drugstore represent single-molecule drugs originally formulated and tested without the benefit of today's AI and ML systems. In the digital era, it is becoming easier to test new, multi-ingredient drug formulations and interpret the results. This advancing AI/ML technology allows researchers to harness the power of plant-based medicines by identifying how multiple ingredients work together to treat serious medical conditions. Robust data analysis can also be used to predict potential side effects from multicomponent plant-based medicines.

Using digital technology to advance its drug design and development, Gb Sciences is tapping into the rich cultural and historical usage of plant-based medicines in TMS across the globe. With the aid of a team of ethnobotanists to address global differences in language and cultures, it created the PhAROS™ Drug Discovery Platform to compile data from across multiple traditional medical systems into a single, searchable engine. This innovation allows for the decoding of plant-based medicines to make modern formulations more user-friendly as it unlocks the potential of plants as a healing source. PhAROS™ can reduce the complexity of traditional medicines based on plant extracts containing hundreds of active ingredients. Using in silico convergence analysis (ISCA), PhAROS™ identifies which ingredients from the original mixtures are the most essential to providing relief. PhAROS™ also finds those ingredients that work together through complementary pathways, which informs the development of the MEM prototypes. Overall, PhAROS™ saves considerable time and money relative to traditional screening processes used for drug discovery.

Currently, Gb Sciences is using PhAROS™ to discover novel disease-targeted MEMs for specific populations of people with unmet medical needs, including complex disorders such as Parkinson's disease, chronic pain, heart disease, anxiety, and cytokine release syndrome. These AI/ML tools can also predict side effects, eventually leading researchers to define parameters to create the correct blend of ingredients that treat specific disease targets while minimizing the potential for negative impacts. This process could be extended to personalized treatments later with the creation of suitably trained algorithms.

Recent Case Studies Support the Benefits of MEMs

Gb Sciences' MEMs represent the future of medicine, which involves creating a "cocktail" of ingredients that can be personalized to achieve optimal outcomes for patients. Gb Sciences is working diligently to refine these MEM formulations in cell and animal models of diseases, intending to advance these studies to human trials soon. Gb Sciences is currently focused on the following development programs:

Parkinson's Disease: To identify therapeutic MEMs for Parkinson's disease from cannabis plants, Gb Sciences used a sequentially reductionist process for creating MEMs that preserves the 'entourage effect' within the whole plant, while generating a simplified mixture that is more replicable by standard pharmaceutical production methods. These MEMs significantly reduced Parkinsonian movement disorders in an animal model. Gb Sciences' MEM are currently being formulated as oral dissolvable tablets to be evaluated in upcoming human clinical trials.

Chronic Pain: Gb Sciences has also deployed its MEM strategy for the treatment of chronic pain. Using the in silico convergence analysis in its PhAROS™ drug discovery platform, researchers evaluated similarities between plant-based active ingredients used to treat pain and inflammation in TMS across different geographic areas. These current MEM prototypes are being tested in animal models and early results support their potential to become effective non-opioid pain therapeutics.

Cytokine Release Syndrome: Gb Sciences used its MEM strategy to find potential treatments for people suffering from the dangerous hyperinflammatory side-effects of viruses like COVID-19. Gb Sciences screened numerous active ingredients from the cannabis plant in inflammatory assays to determine which of these compounds could be used to reduce viral-induced hyperinflammation without causing immune suppression. Gb Sciences found that certain minor cannabinoids and terpenes were able to target specific parts of the inflammatory cascade, whereas tetrahydrocannabinol (THC) led to substantial immune suppression. Gb Sciences has now created MEMs that are designed to downregulate parts of the dangerous hyperinflammatory cascade, while keeping the anti-viral immunity systems intact. These cytokine release syndrome (CRS) MEMs contain two or three ingredients each. Based on the follow-up study performed at Michigan State University, the most effective MEMs have achieved preclinical proof-of-concept for reducing dangerous cytokine storm syndromes, and they are being prepared for further clinical development.

Heart Disease: The plant-inspired ingredients in Gb Sciences' heart disease MEMs can be used to manipulate receptors that protect against and reduce cardiac hypertrophy. Cardiac hypertrophy is a common side effect that occurs as a compensation mechanism with the use of typical single-molecule heart medications. By manipulating calcium channels, these cardiac MEMs developed by Gb Sciences can potentially reduce and reverse hypertrophy in people who suffer from heart disease. Although patents have been granted on these formulations, human trials are currently pending while development partnerships are sought for commercialization.

Anxiety: Gb Sciences' research team has also used the PhAROS™ platform to identify new ingredients to improve upon an initial formulation for anxiety based on a traditional medicine. The original plant-based therapeutic was derived from the kava plant, but some ingredients within kava extracts are thought to cause liver toxicity. PhAROS™ identified ingredients from the related Piper plant family as a substitute for the functionality of the ingredients in question without the potentially adverse safety profiles of those original ingredients. The Piper plant family includes pepper plants that are used worldwide in traditional medicines.

President & CSO of Gb Sciences, Inc., Dr. Andrea Small-Howard, recently announced that Gb Sciences has achieved an important milestone in the development of their novel, kava-inspired anxiety formulations. Not only did some of Gb Sciences anxiety formulations achieve statistical significance in the animal model, but these minimum essential mixtures also demonstrated synergy by significantly outperforming the sum of the activity of the individual active ingredients. This preclinical data also confirms that Gb Sciences' PhAROS™ platform was capable of yielding concrete, potentially effective, plant-inspired combination drugs.

Maintaining a Focus on the Future: AI and MEMs

Gb Sciences is using its PhAROS™ drug discovery platform to create patented formulations that can be offered as alternatives to the single-molecule prescription medications currently available. This plant-inspired biotech combines natural product research with AI and ML technology to develop MEMs, creating an Intellectual Property Portfolio that spans over 60 serious health conditions. To date, six patents for its plant-inspired biotech have been issued in the United States, with another 15 patents-pending. Eight foreign patents have also been issued, with 49 pending. The MEM patents cover composition and use for MEMs whether the active ingredients are derived from plant materials in nature or from synthetically manufactured homologues.

Along with the need for improved therapeutics, the market for treatments of Parkinson's disease is projected to grow to $8.8 billion by the year 2026. Gb Sciences is currently preparing its lead MEM drug candidate for its first-in-human trial. Other plant-inspired biotech activities in their development pipeline include chronic pain trials focusing on time-released capsules using nanoparticles, offering patients up to seven days of relief with a single dose. Gb Sciences is testing its anti-inflammatory MEMs to be used to treat hyperinflammation related to COVID or other viral illnesses. Gb Sciences is also preparing its non-psychedelic, kava-based anxiety formulations to treat the growing global need for anxiety and depression relief.

As a development strategy, MEMs combine the benefits of manufacturing simplicity like single ingredient drugs with improved clinical efficacy like whole plant medicines. Gb Sciences' AI-enabled drug discovery platform allows them to harness the potential of plant-based medicines in traditional medical systems. In addition, PhAROS™ helps predict the potential side effects of a disease and uses them to work for patients instead of against them. By pushing the envelope and working with researchers around the globe, Gb Sciences is amplifying its efforts to promote MEMs as a viable strategy for drug development.

In the next ten years, Gb Sciences' goal is to help shape the future of medicine by using digital resources to rethink how medications are formulated. Complex diseases remain the most difficult to treat; however, MEMs may provide essential solutions for these clinically unmet needs. With the added benefit of pre-analysis for potential side effects, plant-inspired medicines that factor in this data will likely be more effective. Although human diseases are not easily defined, a review of thousands of years of history and the many ways in which plants have been used as treatment options should empower future generations to accept MEMs as the next wave of medicine.

With PhAROS™, Gb Sciences is using digital technology on the front end to unlock the potential of traditional medicines. PhAROS™ guides the discovery of MEMs with three to five ingredients that demonstrate synergy when combined, while also conforming to US FDA standards.To learn more about Gb Sciences and its innovative efforts to transform the future of medicines,

visit https://www.gbsciences.com/.

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