Machines making medicine

Companies use AI to develop new natural products and discover novel applications for familiar ingredients

By Peter Rejcek

In 2020, an artificial intelligence system, dubbed AlphaFold 2, accomplished in days what the most cutting-edge techniques require months or years to unlock—the three-dimensional structure of proteins. Structure is linked to function, so the ability for AI to predict how a protein folds, based on its DNA sequence, means scientists can understand these basic building blocks of life at a scale and speed previously unimaginable.

For starters, AlphaFold 2 could revolutionize the understanding and treatment of some of the most intractable diseases, such as cancer or Alzheimer's. Indeed, one of t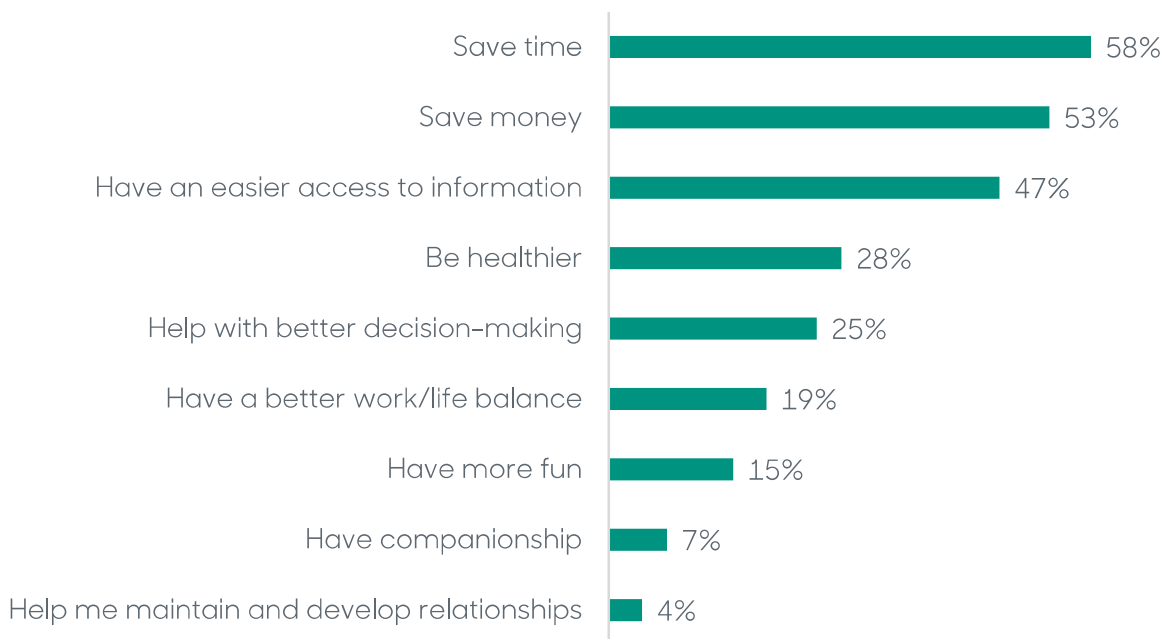he biggest impacts of AI is expected to be in drug discovery and development. Private investment into companies applying machine learning and other AI techniques into therapeutics reached nearly $14 billion last year, according to the Artificial Intelligence Index, a report produced by Stanford University's Institute for Human-Centered Artificial Intelligence.

However, it's not just big pharma that stands to benefit from these sophisticated algorithms, which ingest and train on huge datasets to discern patterns and make predictions. These same advances are being used to identify new phytonutrients or discover novel applications for well-established ingredients in the natural products industry.

NBJ Takeaways

» Artificial intelligence is already at play in pharma and nutritional arenas

» Key mergers and deep investment pockets point toward an acceleration in the field

» Algorithms can connect the dots between health conditions and natural compounds quickly and accurately, significantly shortening product development timelines

REASONS WHY CONSUMERS WOULD USE ARTIFICIAL INTELLIGENCE

Reason	Percentage
Save time	58%
Save money	53%
Have an easier access to information	47%
Be healthier	28%
Help with better decision–making	25%
Have a better work/life balance	19%
Have more fun	15%
Have companionship	7%
Help me maintain and develop relationships	4%

Source: 2018 Gartner consumer AI perceptions study, conducted online during January and February 2018 among 4,019 respondents in the U.S. and the U.K.

"We believe AI is the next generation of scientific tools to help us innovate, not only by identifying new phytonutrients but also by gaining a better understanding of how a compound or ingredient is beneficial," says Tobe Cohen, chief growth officer at **Pharmavite**, which produces the **Nature Made** brand.

shared properties in their active sites," says Nathan Price, Ph.D., co-CEO of Onegevity. "We can then screen against natural products and rapidly identify compounds that are predicted to have effects on various biological targets and processes." Founded in 2018 in partnership with dietary supplements company **Thorne**,

ed to focus on anti-aging formulations, among other applications.

One of the first companies to introduce longevity products based on the recommendation of machine-learning algorithms was **Life Extension**, a supplements company known for anti-aging brand formulations. In 2016, it partnered with a leading AI drug discovery startup, Hong Kong-based **Insilico Medicine**.

Founded in 2014, Insilico has raised more than $50 million toward developing deep-learning technology to identify biomarkers of aging and to create novel drug therapies. The company made headlines in February for using its AI platform to discover both a drug candidate and novel pathway for treating a rare lung disease. It took just $2.7 million and 18 months to validate the small-molecule drug through what is often a much more lengthy and costly pre-clinical phase.

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AI platforms for plants proliferate

The 50-year-old dietary supplements company is embracing that future through a partnership with **Brightseed**, a startup founded in 2017 that recently raised $27 million to build out its plant nutrient discovery platform—Forager.

"The core of Forager, our AI platform, is first about predicting the compounds that exist in plant sources … and then predicting what these compounds would do for a specific health benefit. It's focused on efficacy," explains Sofia Elizondo, Brightseed co-founder and chief operating officer. "We connect the plant kingdom, at a molecular level, to biological health targets and apply AI to predict all of those relationships."

Where Brightseed is focused on building the world's biggest library of plant compounds mapped to benefits, health intelligence company **Onegevity** leverages its large multi-omics database (including transcriptomics, metabolomics and microbiomics) to create high-throughput predictions on its AI platform called Discovery.

"[Discovery] allows us to take biological evidence and chemical structure features to predict natural products that have

Onegevity originally used AI and biometric data to provide personalized wellness recommendations to consumers.

Long on longevity and wellness

The two companies announced a merger earlier this year into **Thorne HealthTech**, not long after Onegevity expanded its portfolio to include business-to-business solutions. One high-profile partnership is with **Indena**, a raw materials supplier in Italy celebrating 100 years in business in 2021, demonstrating that well-established players in the natural products industry see value in the emerging technology. That partnership is expect-

The breadth of data available on the biology of aging, and the pathways involved, has outpaced Life Extension's ability to assess longevity efficacy through clinical trials, according to Andrew Swick, M.S., Ph.D., Life Extension's chief scientific officer. The technology created by Insilico Medicine offered a powerful shortcut to new solutions.

"In order to leverage the longevity pathway data in a relevant and timely manner," Swick says, "we initiated a collaboration with Insilico Medicine so we could combine their outstanding expertise in AI with our deep knowledge of nutraceuticals."

The result of the collaboration is Life Extension's GEROPROTEC line of anti-aging formulas. In 2017, it introduced both Ageless Cell, a formulation of four

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specific nutrients—myricetin, NAC, gamma tocotrienol and EGCG—that reputedly inhibit cellular aging, and Longevity A.I., which combines withaferin a, gamma-linolenic acid, and ginsenoside Rg3 (from Asian ginseng) to mimic the metabolic benefits associated with calorie-restrictive diets.

The need for speed

While the computer code and scientific research underpinning these platforms are highly technical and are still works in progress, the value proposition is pretty simple: algorithms can connect the dots between health conditions and natural compounds at a speed and confidence level that significantly shortens the development phase of new wellness products.

For example, taking a "grind-and-find" approach to work through botanical libraries could take years. Companies like Brightseed claim to condense the matchmaking search between benefit and compound—and vice versa—down to months. Speed is built on data and processing power. In the case of Forager, the platform will have mapped more than a million plant compounds by the end of 2021, according to Elizondo.

A company spun out of Georgia Tech called **efficacyAI** claims its drug discovery platform, MedicascyAI (rhymes with efficacy), can link a health benefit to a natural ingredient in just weeks. Co-founder Jeff Skolnick, Ph.D., has spent the better part of 15 years developing algorithms capable of making these analyses based solely on the chemical structure of the molecule and then drawing on a target prediction library that contains 97% of all human protein sequences.

MedicascyAI generates confidence levels as high as 80% that a small molecule, whether it's a drug or botanical compound, will be safe and effective. "You can target key pathways that are associated, say, with energy production. You can map these things to mood, mental acuity—what's the logical equivalent of a wellness prediction, in addition to mapping of a disease indication prediction," Skolnick says.

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Algorithms aren't just for allopathic medicine

Southwest College of Naturopathic Medicine brings 21st century technology to traditional herbalism

Just because naturopathic medicine approaches health from traditional practices doesn't mean practitioners have turned their backs on the high-tech tools available to them today, including the promising computing power of artificial intelligence.

That convergence of the old and the new is taking physical shape at the Southwest College of Naturopathic Medicine, which is scheduled to complete construction of a state-of-the-art molecular biology and phytochemistry laboratory in 2021, as part of an expansion of the Ric Scalzo Institute for Botanical Research. The new facility will bring a more rigorous scientific approach to developing natural products by studying the molecular underpinnings of plant extracts in order to understand the link between compounds and biological pathways.

"That's really what we feel has been missing from natural products research," says Bill Chioffi, vice president of strategic partnerships and business development for the institute. "People are testing clinically, in patients, formulas that haven't really been well developed on the back-end."

Chioffi says the lab is approaching the task of product innovation with the mindset of a startup, building partnerships in both industry and academia. And part of that approach is leveraging new tools like artificial intelligence to deliver data-driven insights at a scale and speed beyond human capabilities.

"No scientist actually can keep up with the [scientific] literature nowadays," notes Susan Trapp, Ph.D., who recently joined the institute as an expert in molecular biology, genomics (including research on the Human Genome Project)

and computational biology.

The latter is a scientific discipline that uses mathematical models to understand biological systems. AI and computational biology are merging, to the extent that the terms are sometimes used interchangeably when speaking about algorithms that ingest and analyze large datasets.

Take the example of echinacea, a popular dietary supplement that is marketed for a number of health conditions, using various parts of the plants, across a wide variety of formulations. An algorithm trained to sift through the scientific literature and other sources could quickly make predictions about optimal extractions for the kind of product desired.

"All of those factors can be sorted through with AI from the reams of data that's out there about echinacea already," Chioffi says.

Trapp says the nutraceuticals industry is still in its infancy compared to big pharma regarding the use of AI, computational biology, bioassays and other advanced lab techniques for developing new products. "We're probably five to 10 years behind [when] utilizing all of these tools," she says.

Chioffi says he believes the institute can help bring scientific rigor to the natural products industry and instill a thirst for research in the wider naturopathic community.

"Our great hope would be to work with manufacturers of botanical extracts to improve what's being put out into the supply chain," he says. "We're really hoping to inspire the next generation of naturopaths to look at research as an avenue for their work."

ments," he added, "but it can save you a lot of time and energy and tell you which experiments you should do."

AI already identifying potential products

There is certainly hope—and no small amount of hype—for what AI can do in helping design new products or discovering novel applications for existing ones.

In January, for instance, Brightseed announced its first AI-powered discovery for metabolic health: two compounds, found in more than 80 edible plant sources, that help clear fat from the liver. Forager helped further narrow the search by identifying which plant source is most sustainable and best expresses the compounds for extraction, among other criteria. One such source is black pepper, according to Elizondo.

The company is also working with **Danone North America** to identify plant compounds in the food giant's raw soy that could provide previously unknown health benefits and claims.

In the case of MedicascyAI, the platform flagged a novel use of caffeine as a topical remedy for fungus, according to Skolnick. "That's an example of a really beaten-to-death molecule that the algorithm predicted," he says. "This is a massive hypothesis generator, which obviously has to be validated. I'm not saying it can't be, but it gives you a short list of things to do. And that's the power of it."

The dietary supplements industry even holds something of an advantage over traditional pharmaceuticals, Elizondo notes, because plant sources tend to have a much more robust safety profile than synthetic compounds.

"The big advantage in the natural products space," notes Price at Onegevity, "is that compounds that are generally recognized as safe ... do not have the same regulatory approval process as do drugs and therefore can be moved quickly into trials to test efficacy."

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Can AI offer a personal touch?

Not surprisingly, Price says he believes there is "massive potential" for AI in the natural products industry that could stretch into offering personalized solutions. "Despite current health solutions continuing on a 'one-size fits all' approach, we have seen an increased demand for personalization, as people are seeing the benefits of better health outcomes," he says. "We have developed our sophisticated AI system to utilize pattern recognition, deep neural networks and bioinformatics to deliver unparalleled molecular insights and personalization."

Not everyone is convinced that AI can

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so easily solve the personalization wellness challenge, however.

"I think we all got really excited about personalized health, because suddenly you can spit in a test tube and get genomic information, and that's super cool," Elizondo says. "What we're missing is the same level of detail from what we eat."

When people eat plants today, she continues, we're lucky if we know the vitamin and mineral content, let alone the phytonutrient content in the foods we ingest. She notes that the majority of FDA-approved small-molecule drugs are derived from these powerful phytonutrients in plants. "Without having the molecular-level visibility, there is no way that you can personalize nutrition," Elizondo says.

Skolnick says he believes personalization is possible, but that it has a long way to go. The algorithms are optimized for the average human, he explains, and can't account for individual metabolic rates or other factors without more extensive biometric data. "If you are talking about personalized nutraceuticals, we need, at the very least, genotyping and probably some kind of epigenetic information in order to say something intelligent," he says.

Leveraging AI is not about chasing consumer trends, according to Cohen at Pharmavite. "It's about leveraging technology and innovation to help consumers achieve the health and wellness outcomes they're striving for. It goes beyond what's happening in our industry at this moment and looks down the road at novel phytonutrients and compounds that could positively impact health in ways we can't even imagine right now."