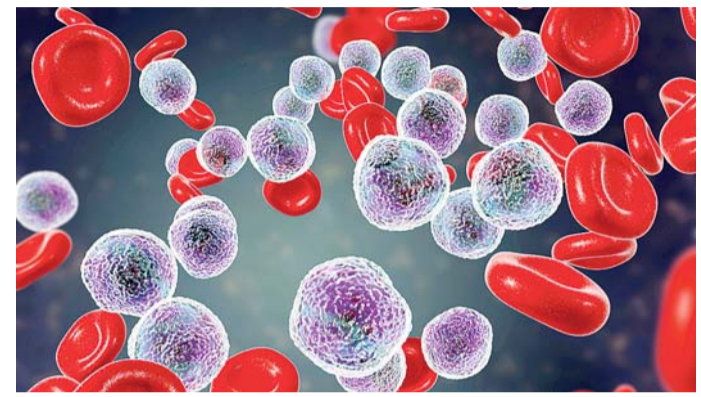


## #PHARMACOLOGY

### New Leukaemia Killing Compounds



Dozens to thousands of mitochondria are at work every minute in every living cell and like all machines they wear out with use.

Researchers from Rice University and the University of Texas MD Anderson Cancer Centre have discovered potential new drugs that work in concert with other drugs to deliver a deadly one-two punch to leukaemia.

In previous studies, the research groups of Rice chemist Natasha Kirienko and MD Anderson physician-scientist Kirienko screened some 45,000 small-molecule compounds to find a few that targeted mitochondria. In the new study, they chose eight of the most promising compounds, identified between five and 30 closely related analogues for each and conducted tens of thousands of tests to systematically determine how toxic each analogue was to leukaemia cells, both when administered individually or in combination with existing chemotherapy drugs like doxorubicin.

"One of the big challenges was to establish optimal conditions and doses for testing on both cancer cells and healthy cells," said study lead author Svetlana Panina, a researcher at the University of Texas at Austin who conducted the research during her postdoctoral studies at Rice. "The results from our previously published cytotoxicity assay were helpful but very little is known about these small-molecule compounds and how they have been thoroughly described in other studies and we had to essentially start from scratch to determine how much to use, what they do in cells, everything. All the doses and treatment conditions had to be adjusted by multiple preliminary experiments."

In prior work, Kirienko's lab had shown the eight compounds targeted energy-producing machinery inside cells called mitochondria. Dozens to thousands of mitochondria are at work every minute in every living cell and like all machines they wear out with use. The eight compounds induce mitophagy, the house-keeping routine cells use to decommission and recycle mitochondria that are past their prime.

During times of extreme stress cells can temporarily forgo mitophagy to get an emergency energy boost. Cancer is notorious for hijacking these sorts of programs to fuel pathological growth. For example, previous research has shown leukaemia cells have far more damaged mitochondria than healthy cells and are also more sensitive to mitochondrial damage than

healthy cells. Kirienko and Konopleva reasoned that mitophagy-inducing drugs might weaken leukaemia cells and make them more susceptible to chemotherapy.

"We hypothesized that if they activate mitophagy, they may be particularly toxic to leukaemia cells," said Kirienko, the corresponding author of the new study. "And indeed, we found that six of the eight small-molecule compounds were deadly to leukaemia cells. We then wanted to study them more in depth. So we looked at closely related molecules, and we looked at combinations."

When two or more drugs are given in combination, researchers can also administer them individually and compare the effectiveness of each regimen.

"There is a number called synergy coefficient that quantifies interactions between drugs," Kirienko said. "If the coefficient is negative, the drugs are antagonistic and work against one another. Zero means no effect, and positive numbers indicate positive interactions. Anything above 10 is considered synergistic."

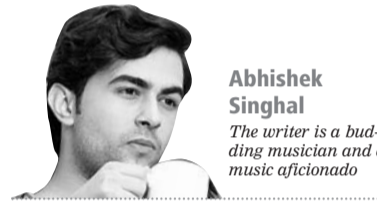
For example, one currently prescribed drug combination for leukaemia - doxorubicin and cytarabine - has a synergy coefficient of 13, Kirienko said. The team's experiments showed several mitophagy-inducing compounds were significantly more synergistic with doxorubicin. The most synergistic compound, PSI27B, had a coefficient of 29.

"The point of synergy is that there are concentrations, or dosages, where a single drug doesn't kill," Kirienko said. "There is no death of healthy cells or cancer cells. But administering those same concentrations in combination can kill a considerable amount of cancer cells and still not affect healthy cells."

"We started by testing the toxicity of its mitophagy-inducing compounds and combinations against Acute Myeloid Leukaemia (AML) cells, the most commonly diagnosed form of the disease. They then tested the six most effective AML-killing compounds against other forms of leukaemia and found five were also effective at killing acute lymphoblastic leukaemia (ALL) cells and Chronic Myelogenous Leukaemia (CML) cells. Control studies found all the mitophagy-inducing drugs caused far less harm to healthy cells.

In their final experiments, the researchers tested one of the most effective mitochondria-targeting compounds, PSI27E, using a cutting-edge technique called a patient-derived xenograft (PDX) model. In PDX, also referred to as a "mouse clinical trial," mice are implanted with cancer cells from a leukaemia patient. Once the cells grow the mouse is exposed to a drug or combination of drugs as a closer-than-cells test of the treatment's effect. PDX tests on one compound, PSI27E, showed it was effective at killing AML cells in mice.

When a traditionalist information and broadcasting minister of India banned film songs on the national radio in a fear that they would 'corrupt' the youth of the country, Radio Ceylon rose to the occasion with 'Binaca Geetmala' and became the hot favourite of the Indian masses.



Abhishek Singhal  
The writer is a budding musician and a music aficionado.

# When Ceylon Stepped In To Save Our Music



Lata Mangeshkar with Kishore Kumar at a recording.

## #RADIO CEYLON

It was in 1952 that the minister of Information and Broadcasting (I&B) of newly independent India, BV Keskar, decided that All India Radio (AIR) the information and entertainment lifeline of the nation would not air film songs as they were degenerated and far too 'Westernized'. He believed they would hinder the cultural growth of a young nation on the cusp of a bright future. Instead, he proposed, the country could lend its ears to hallowed classical music.

### A Corrupting Influence

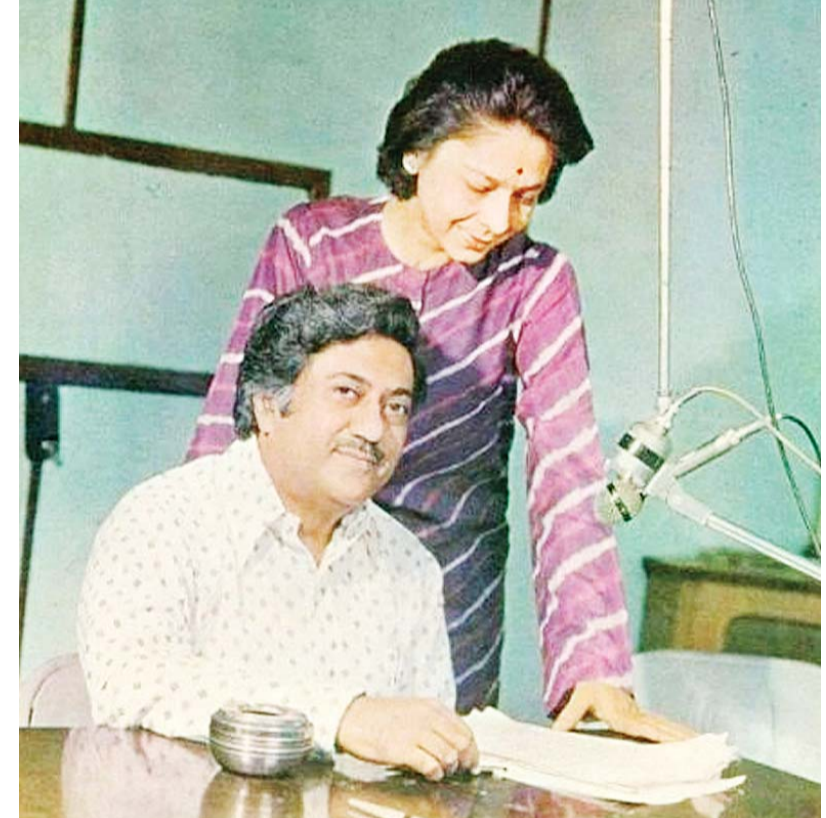
In an article in The Hindu (19 July 1953), Keskar argued that the country's appreciation for classical music had 'fallen' and was 'on the point of extinction' - particularly in north India. The onus of making his countrymen 'intimate with classical music' it was therefore bestowed on AIR. "We must make (ourselves) familiar with our traditional music," he declared.

In 1952, the Indian National Congress party just had a landslide victory in the first general election, and Keskar - a staunch Brahmin and a classical Indian music purist - was given charge of the I&B ministry.

To begin with he mandated that all songs aired on AIR would be screened and according to Lelyveld, he imposed a quota of 10 percent of all program time". In addition, Keskar ensured that if a film song was played the film's title would not be announced since he considered that advertising. Only the singer's name would be mentioned.



Ameen Sayani.



Ameen Sayani with his wife Rama Sayani.

### Film Music Ousted

The film industry was up in arms of course. Filmfare magazine characterized Keskar as a 'devils man' whose decision was 'a calculated blow at the reputation of the Indian film industry, as much as one aimed at ousting film music from the market' (August 1952 issue). In response, the film producers who owned the rights to the songs decided to rescind the broadcast licences given to AIR. And as Keskar anticipated, film music completely disappeared from radio within a mere three months. The void was filled by AIR broadcasting classical music.

### Radio Ceylon to the Rescue

Across the shore, Radio Ceylon rose to the occasion and the opportunity. The radio station was launched in December 1925, just three years after BBC, under strict British laws. During the later years of the Second World War, the Allied South East Asia command under Lord Mountbatten set up an extremely powerful transmission capability in

soon set the benchmark and enjoyed immense popularity because of its long reach and clear sound. Sir Edmund Hillary, the then High Commissioner of New Zealand in New Delhi, once stated that when Tenzing and he were on Mount Everest, the only station they could receive was Radio Ceylon.

### Binaca Geetmala

As Radio Ceylon's popularity grew in India, Keskar's influence waned and the government was forced to lift the ban. In 1957, Vividh Bharati was conceptualized as a service on AIR that offered non-stop film music broadcast. "Vividh Bharati had a tremendous blend of heritage and modernity, pampara and pragati, let's say. And this soon became quite popular," noted Sayani in the 2010 interview. By 1967, Vividh Bharati had turned commercial and began accepting advertisements. By the late 1970s, it had become a cultural behemoth, functioning as the primary source of entertainment in Indian cities.

Keskar would be outraged if he heard the music the Indian film industry makes today, but it is ironic that some of the country's most iconic and memorable songs produced during the 'golden era of Hindi cinema' were once considered objectionable and would have possibly been stifled by one man's draconian policies if a radio channel from a neighbouring country hadn't stepped in.

Sometimes, we did get into trouble, especially with Geetmala, because with Geetmala we were not supposed to record too much in advance. The popularity poll had to reflect a current mood... (Binaca Geetmala) became an absolute rage. Just like how the streets would be empty when BR Chopra's Mahabharat (1988) or Ramanand Sagar's Ramayan (1986) would be on television, the same thing happened to Geetmala... Wednesdays came to be known as Geetmala day."

### The Ban Lifted

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### Geetmala Day

In 2010, Sayani, in an interview with Aswin Punathambekar (professor of communication studies at the University of Michigan-Ann Arbor), recounted how his team would record the show on tapes, "every single day. And every week's quota used to fly by Swiss Air. Air Ceylon or Air India to Colombo.



Sunil Dutt listening to Hindi film star Nalini Jaywant speaking over Radio Ceylon.



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### The Era of Songs

A former editor of Femina, Sathya Saran, who was a young girl growing up in Guwahati at the time, recalls what the show meant to her. "Every Wednesday, I would go and sit near the radio from 8-9 pm to listen to Binaca Geetmala," she reminisces over the phone. "I had this little black diary in which I wrote down every song that played, how many times it was featured, whether it had gone up or down; I would keep tabs and would always sing along because I knew all the lyrics. And Ameen Sayani was like God to me. I would hang on to every word he said." Geetmala ran from 1952 to 1988.

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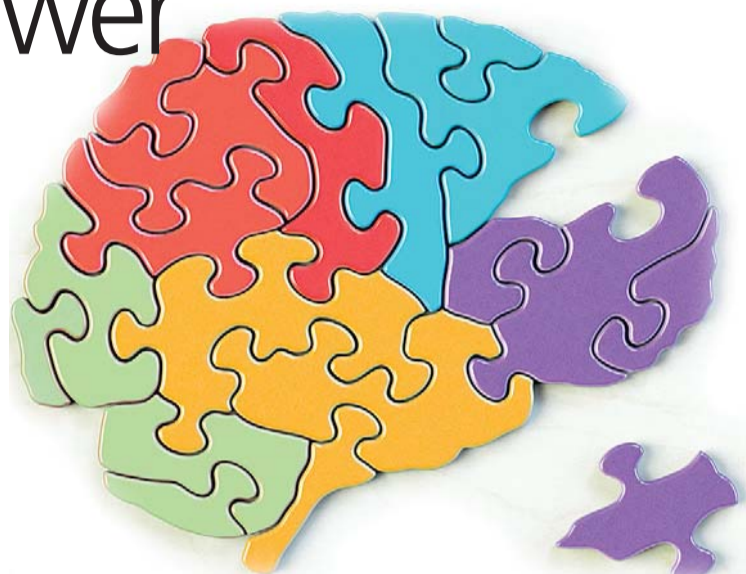
## Holistic Therapy Day

Western medicine has been considered to have some rather severe issues when viewed from other forms of medical practice throughout the world. Holistic Therapy is one such practice that focuses on the body, spirit and mind and uses these three factors working in conjunction to help promote natural healing in the body without unnecessary procedures or medication. Holistic Therapy is your opportunity to learn more about this alternative medicine and how it can make essential changes in your life.

## #BRAIN GAMES

# How to Boost Your Brain Power

When it comes to recall, it's very much a case of 'use it, don't lose it'. Here's how you can improve yours at any age...



Improving your long-term and working memory can improve your performance by boosting your productivity, as well as decision making and organizational skills. It also reduces stress which can further improve performance and overall happiness at work. Improving your memory requires time and regular exercise of the brain.

In this article, we will discuss memory games and how you can use them to boost your memory as well as other tips for improving brain function.

### What Are Memory Games?

Memory games are a fun method of exercising your mind to improve your memory. Like our bodies the brain needs regular use to stay healthy and sharp. Memory games challenge the mind and help the gray matter in our brains the part that impacts memory - to grow and expand. Research has shown that just 15 minutes each day of brain training can improve brain function. Here are the top games you can play to improve your memory.

### Crossword Puzzles

Crosswords are one of the most classic brain training games. These games can help test your vocabulary skills and draw on knowledge from history, science and popular culture. You can perform crosswords online or through gaming apps or go with the more traditional route such as printed books or newspapers. Crosswords are often used as a cognitive exercise to delay the onset of dementia especially when made into a regular habit. Focus on puzzles that are challenging and keep your brain engaged. Because it's possible to strain your brain, limit yourself to one challenging puzzle per day.

### Chess

The game of chess was designed to be a mentally intensive and intellectually challenging game. It requires reliance on short-term memory to fully analyse the board and create a strategy for each move. You will also have to anticipate the moves of your opponent and make sure each

### Concentration

Concentration is a popular game used to help children develop memory and retention skills. In this game you lay any number of cards face down and then flip

two at a time trying to match sets. To increase the difficulty of the game and challenge your brain more, opt for the 'spaghetti variation', where the cards are in a messier arrangement. The less orderly layout will make it more challenging to remember where the cards are and increase the level of difficulty for your brain.

### Jigsaw Puzzles

Jigsaw puzzles are effective brain training games, as they require you to work the left and right sides of the brain at once. They also reinforce the connections between the brain cells which improves mental speed and improves short-term memory. Jigsaw puzzles reinforce visual-spatial reasoning as well as you need to look at the individual pieces and identify where they fit into the big picture.

### Rebus puzzles

A Rebus puzzle works well for improving memory and brainpower. This puzzle asks a question and then the clues to the answer are found in numbers, letters, pictures and symbols. Players must have knowledge of and be able to remember clichés and expressions to solve the puzzles.

### Sudoku

Sudoku can help improve your memory retrieval and stimulate other parts of your brain. To successfully complete this game you are required to keep a range of numbers in your head while placing them mentally in one of the nine spaces on the grid. This game relies heavily on working memory to memorize the numbers and then uses logical thinking to figure out the next blank.

Because Sudoku requires players to think strategically and use creative thinking to solve problems, it can help to increase both concentration and problem-solving skills. Players learn how to make decisions and take action with less hesitation.

### Meditate

Research has shown that meditation increases the gray matter in the brain, the part of the brain that impacts memory and cognition. Meditation and relaxation techniques have shown improvement in the short-term memory for people of all ages.

### Get Enough Sleep

Sleep plays an important role in memory consolidation, the process in which short-term memories are transformed into long-term. Experts recommend between seven and nine hours of sleep each night for adults.

### Exercise

Research has shown that exercise may improve the growth and development of neurons which leads to improved brain health.

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### Multi-tasking Games

Consider choosing games that require you to multitask. This can help you improve your working memory and recall the necessary information when needed to solve a problem. By doing this, your neural markers will be modulated which can train your



brain better to cope with distractions and interference in the midst of retrieving information. Video games are actually excellent for boosting brain power by improving multitasking skills.

Here are a few extra tips to help you improve your memory for better performance in the workplace.

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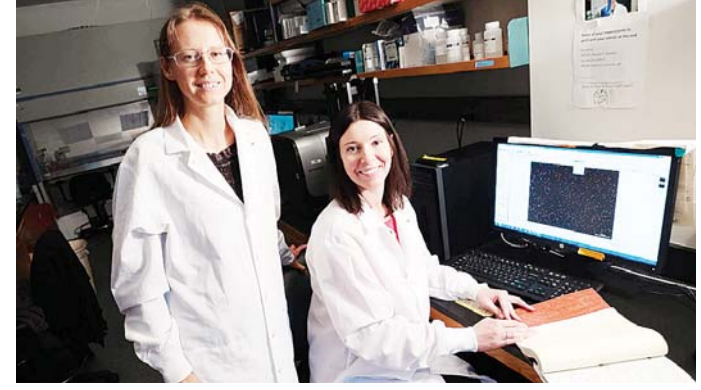
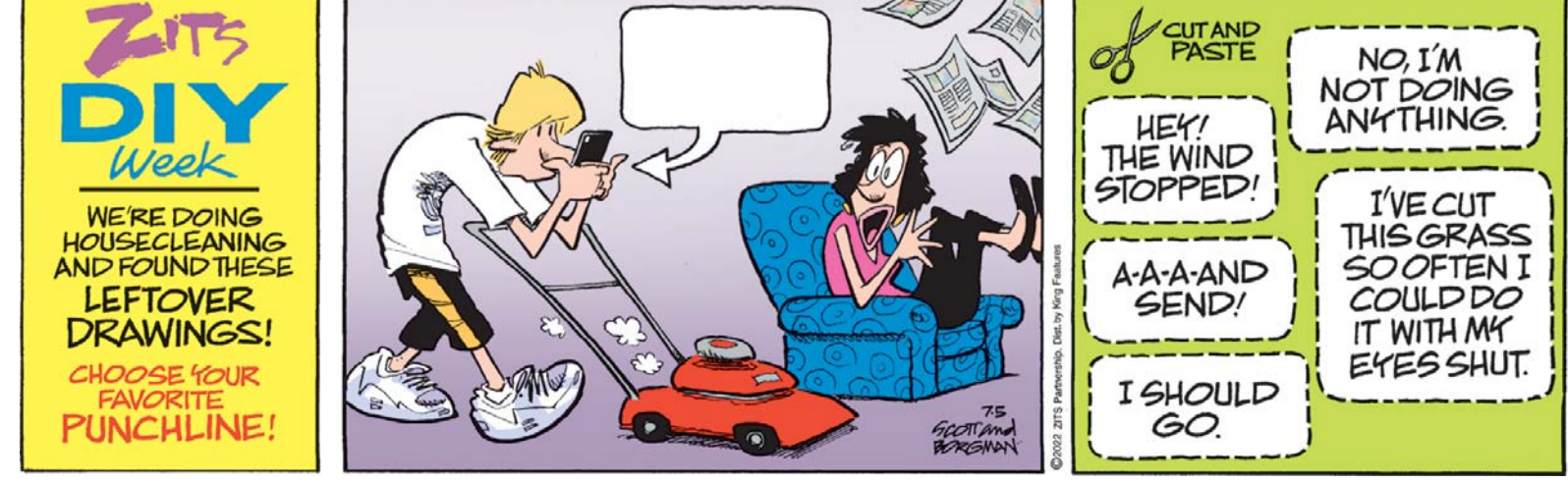
## THE WALL



## BABY BLUES



## ZITS



By Rick Kirkman & Jerry Scott

By Jerry Scott & Jim Borgman