The unexpected healing properties of carbon monoxide gas

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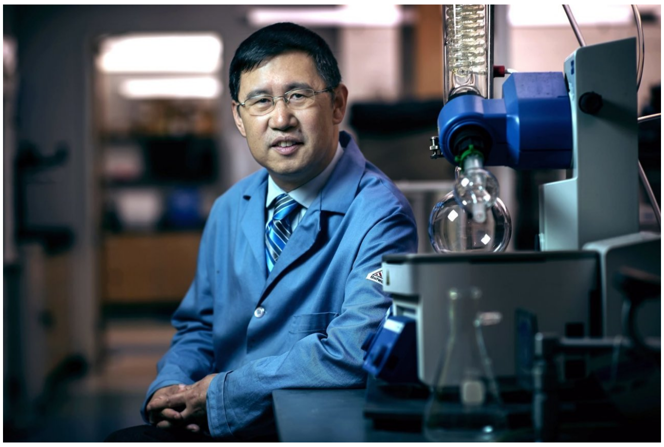

Credit: LaTina Emerson

When most of us hear the words "carbon monoxide," our first instinct is to probably hold our breath. Yes, the colorless, odorless gas can kill you if you breathe too much of it, but according to Dr. Binghe Wang, Regents' Professor of Chemistry and director of the Center for Diagnostics & Therapeutics, carbon monoxide gets a bad rap. He's studying how the gas can be used as a therapeutic agent to treat diseases such as lupus, rheumatoid arthritis, colitis and cancers.

Below he shares how he's using carbon monoxide as a medical treatment:

Q: Most people consider carbon monoxide to be toxic and hazardous, but you've found that it has good qualities. Why is carbon monoxide important to humans?

A: We produce carbon monoxide all the time. It's what's called a gasotransmitter—gaseous molecules that play very important physiological roles in mammals. Among them are three molecules: carbon monoxide, hydrogen sulfide and nitric oxide. If we didn't have those three gases in our system, we would die.

Q: What medical illnesses can be treated with carbon monoxide?

A: There have been a lot of studies on carbon monoxide's therapeutic effect in treating inflammatory conditions. It is very effective in inhibiting systemic inflammatory responses, which are conditions commonly seen in diseases such as lupus and rheumatoid arthritis, and infection, including sepsis.

In addition, organ transplantation studies have found that administering carbon monoxide to the subject improves the survival rate of patients and decreases inflammatory response. It's also a very important molecule in regulating our immune responses. A lot of animal studies also clearly show carbon monoxide can be used to treat colitis.

Q: Since our bodies need carbon monoxide, how can it kill us?

A: The safety margin for carbon monoxide, meaning the difference in the level that would have life-threatening risks and the level that affords therapeutic effect, is actually higher than for glucose or insulin. So, it's only toxic at a very high level. Carbon monoxide binds to iron-containing molecules in the body, mostly hemoglobin. Hemoglobin is very important in transporting oxygen to various locations in our body. Carbon monoxide kills because it binds to hemoglobin and then blocks or inhibits its ability to carry oxygen.

We can tolerate a fairly high level of carbon monoxide without a detrimental effect to our body. It can kill by overwhelming our respiratory system.

Q: How can it be administered as a medical treatment?

A: Most of the earlier studies used an inhaled form of carbon monoxide. That works really well in lab experiments, but it's very hard to imagine a therapeutic form in which a patient carries a tank of gas everywhere so they can take a few puffs once in a while.

So, there has been a lot of interest in developing different delivery forms of carbon monoxide. What we're working on is to make carbon monoxide into a pill. A person can take it orally with a very well defined dose, or it could be dissolved in a solution for intravenous therapy or injection. We have published a number of papers in this area.

Q: Can you describe the carbon monoxide drugs you're developing?

A: We have made different types of carbon monoxide "prodrugs." A prodrug is the precursor of a drug and must undergo a chemical conversion before becoming an active pharmacological agent. For one prodrug we made, once it goes into the blood stream or the gastrointestinal (GI) system, it would start releasing carbon monoxide. By simply putting it in water, it would start releasing carbon monoxide. But otherwise, it's a solid tablet form.

Then we also have other prodrugs that can release carbon monoxide based on pH, a measure of the acidity or basicity of a solution. We have one that is stable in the stomach, but once you get into the lower GI where the pH is higher, it will start releasing carbon monoxide.

We also have a prodrug system that will release carbon monoxide in the presence of reactive oxygen species, which are unstable molecules that contain oxygen and easily react with other molecules, and may cause damage or cell death. There are two types of tissues that have elevated levels of reactive oxygen species—inflamed tissues and cancerous tissues. We can use reactive oxygen species to trigger the release of carbon monoxide. We have found that carbon monoxide can make cancer cells more sensitive to traditional chemotherapeutic agents. That way you don't have to use as much. Or you can use the same amount and it will kill many, many more cancer cells.

We recently found that if you administer carbon monoxide together with an antibiotic called metronidazole, it can sensitize bacteria toward the same antibiotic by 25-fold. It makes the bacteria much, much more sensitive to the antibiotic.

Q: What's your biggest challenge in doing research on carbon monoxide?

A: I always say one of the remaining problems that we have to overcome is the perception that carbon monoxide is very toxic. It's actually not, at least not at the level needed for its therapeutic effect.

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