Research into tamoxifen delivery has special meaning for breast cancer patients

Current research being conducted at Idaho State University into the delivery method of the drug tamoxifen could mean fewer side effects for breast cancer patients and could have applications to more toxic drugs used in cancer treatment.

This is the early forecast by ISU researchers Dr. Nandita Das, principal investigator, and co-investigators Dr. Sudip Das and Dr. Cindy Wilson.

Tamoxifen is one of the oldest, most widely prescribed and successful therapies known for the treatment of estrogen receptor positive breast cancers. It is also FDA approved for the prevention of breast cancer in high-risk patients. Targeting the drug to the body’s lymphatic system could improve the drug’s cancer-fighting abilities.

“Lymphatic vessels are present alongside blood vessels and serve as important agents in the body’s defense mechanism because they filter out organisms that cause disease, produce certain white blood cells, and generate antibodies,” noted Nandita Das. “They also drain off excess fluids and protein so that tissues in our bodies do not swell.

“Unfortunately,” she added, “the lymphatic system also serves as the medium for metastasis, the invasion of cancer from an isolated location through the rest of the body.”

According to Nandita, “Due to the lack of a pumping mechanism, lymph flows very slowly compared with blood. If we could localize anti-cancer drugs within lymph vessels and lymph nodes, the drug would stay in place for long periods of time, allowing for greater chances of interacting with and killing cancer cells that are floating around in the lymph, thus potentially preventing metastasis.”

A rich network of lymph vessels and lymph nodes exists in and around the human breast, so localization of the drug within the lymphatic system could also target drug delivery to tumors.

“The goal of targeted drug delivery is to preferentially concentrate a large proportion of the drug dose in the vicinity of the target tissue, for example a tumor, while sparing the rest of the body from the drug as much as possible. This could greatly reduce side effects and toxicities related to drugs,” Nandita said.

“One highlight of the project is the possibility of achieving drug targeting by simple oral dosing, which would be very convenient for patients,” said Sudip. “Our unique drug delivery approach, called self-emulsifying drug delivery systems and using specialized FDA approved ingredients, will allow the drug to be channeled toward the lymphatic system in preference to direct absorption into the blood vessels from the gastrointestinal tract.”

The Dases and Wilson are bridging the gap between two main branches of pharmaceutical science and research — pharmacology, the study of the effects of drugs, and pharmaceutics, developing ways to put a drug

Cancer patient eager for treatment’s possibilities

ISU pharmacy professors Drs. Nandita Das, Sudip Das and Cindy Wilson have a fan they never met, one who read a news article this fall in the Idaho State Journal about their tamoxifen research.

“If the ISU researchers could get even a partial breakthrough in their studies of tamoxifen so that it is not so risky to take, so that you’re not poisoning your entire body to save part of it, it would be wonderful,” said Colleen Settell, 45, a senior in international studies who works for ISU as a Spanish tutor and tutor coordinator for Content Area Tutoring — and who was diagnosed with breast cancer in 2001.

“I was as devastated as you can get when I received the diagnosis,” Settell said. After a biopsy of the lump in her breast, the tumor was surgically removed, along with about a dozen lymph nodes under her arm.

To prevent a recurrence of the cancer, she began a treatment regimen of three months of chemotherapy, six weeks of radiation therapy, and another three months of chemotherapy. The intense chemotherapy was the most challenging and uncomfortable part of her treatment.

“I received a combination of three drugs and had horrible side effects during that period. It was two weeks on, two weeks off. Basically your body is killed off for two weeks at a time and you recover for two weeks,” Colleen said. “It was absolutely the worst part of my treatment, but what I went through was nothing compared to what other patients went through.

“I didn’t lose my hair,” she continued. “I wasn’t so sick I couldn’t move; I wasn’t puking all of the time. Chemotherapy is a horrid way to save someone’s life. I was pushed to my limit, and it still wasn’t that bad compared to what I saw around me.”

Her radiation therapy was five days a week for six weeks. Each time she was zapped, the whole process took about a half hour, although she received radiation for only about two minutes.

Since her last bout of intensive chemotherapy, she has been taking tamoxifen in pill form twice daily. Again, she counts herself lucky, saying the side effects from the drug she takes “are relatively minimal.” The major side effect is intense hot flashes.

“You feel like you might spontaneously combust when one comes on,” she noted, with a laugh.

The hot flashes increased dramatically in severity and frequency when she began taking tamoxifen. They still visit her regularly, often daily, but they are less intense, and Settell said she is better at managing them now. When she feels one coming on, she heads outside when it is cold, finds a fan to stand in front of, disrobes as much as appropriate in the situation she is in, and finds other ways to cool off.

She recalls reading the warnings associated with the drug tamoxifen and the warnings she has received from physicians. One possible side effect is cancer of the endometrium. Settell wasn’t thrilled when she heard that.

“They told me by protecting myself from not getting breast cancer again that I might be giving myself another type of cancer. Great,” she said.

In late November Settell had a checkup and a mammogram, which was clear. She has a clean bill of health for now.

“The cancer experience is always on the back of my mind, but I don’t dwell on it,” she said. “I see life very differently than I did before I found out I had cancer. It changed the way I look at the world, experience life, everything.”

Keeping a sense of humor throughout the entire ordeal has helped. “If I hadn’t laughed through cancer treatment, I would have died of despair,” she said.
in dosage form, making it usable with a minimum of side effects. "A lot of people may not be aware that when they take a drug, there is a whole area of science behind making sure the drug actually gets into a person's system and does what it is supposed to do," said pharmacy dean Dr. Joseph Steiner.

The researchers are optimistic that the outcome of the study will lead to more funding from the National Institutes of Health, which gave the trio $128,820 for their research. This is one of the few NIH grants the College of Pharmacy and ISU, in general, have received.

The Dases are specialists in drug delivery. Wilson’s primary training is in pharmacology and physiology, studying the effect of drugs. "The fact we received NIH funding for this project on the first try is very exciting," Wilson said. "It is a collaborative effort and a chance for me to utilize my expertise towards drug delivery, which is not my area. At the same time I’ll gain experience and knowledge in a new field. This collaboration expands my research into an area I could not do with my previous training. I can help the Dases, and ultimately they can help me, not specifically from this grant, but from the collaboration we’re establishing."

"Receiving an NIH grant brings national recognition to ISU," Nandita said. "And once you get one, it can open up doors to get more NIH grants."

Pharmacy professors Drs. Sudip and Nandita Das share a 12-year marriage, research projects at ISU, a 4-year-old son, Rishi, and an Indian heritage and upbringing. They thrive off each other’s personalities, differences, passions and interests. Sometimes after a day at work, they head home, each to their own computers, and continue to work. "Our teamwork goes beyond the work we do at the college. We are constantly working on projects together," Nandita said. "That would make some people unhappy, but you don’t achieve as much if you don’t work hard, and we are a strong team. We produce more collectively than we would individually — it’s synergistic."

"They are a dynamic duo," said Dr. Joseph Steiner, pharmacy dean. "They work very hard for the college, and it is unique to have two family members sharing the same research efforts in pharmaceutics, which is an important area for our professional and graduate programs."

"I think they have a unique collaboration as scientists that is enhanced further by their personal collaboration," said Dr. Cindy Wilson, co-investigator in their tamoxifen research project and colleague in the pharmacy college. "They balance each other well, and their collaboration as scientists allows them to bring much more to their careers, the college and the university as a whole. It’s much easier for me to collaborate with faculty across the hall than across the country. They came to ISU with that ability already built in."

The Dases are both from India. Sudip was raised in Calcutta, India’s second largest city, population 12 million, and Nandita was raised in north India’s Varanasi, the holiest of Hindu cities, where pilgrims commonly go to worship. "Average individual income per family is very low so India is categorized as a poor country," Nandita said. "On the other hand the happiness you will see there with the people with no money is amazing — that’s a spiritual experience you get when you don’t need money to be happy and are removed from materialistic needs. It is a happy country."

India is also a technologically advanced country with a highly educated workforce that is attracting investment in high-tech industries all over the world.

The couple met at a national research conference in Calcutta. Sudip had just finished his Ph.D. They married in 1991, and the next five years they primarily lived apart. From 1990-95, Nandita earned her Ph.D. in pharmaceutics at the University of Pittsburgh, Pa., part of the time working as a research scholar at SmithKline Beecham Pharmaceuticals.

In the meantime, Sudip finished a postdoctoral fellowship in pharmaceutics at the University of Queensland, Brisbane, Australia; taught first at Memorial University of Newfoundland, St. John’s, Canada; and moved to Nova Southeastern University, Ft. Lauderdale, Fla. In 1995 Nandita joined Sudip in Florida and taught and practiced pharmacy for three years before the couple came to ISU in 1998.

Both have accomplished careers as teachers and researchers, and are widely published. They both work on a variety of research projects as well as teaching full loads. Their 4-year-old son, Rishi, was born in Idaho and is already showing signs of being a scholar. "He is already interested in books and we’re seeing indications for an academic bent early in his life," Sudip noted.

Rishi’s other love is animals, which perhaps started with a drive through the African Lion Safari, a commercial wildlife park near Toronto, Canada, where he was two years old. The Dases have memberships to the Pocatello Zoo and the Hogle Zoo in Salt Lake City. With busy careers and home life, the Dases have not been able to go to India since Rishi’s first birthday. Nonetheless, they retain ties with their culture, communicating frequently with family and friends in India, interacting with Indian students and being involved with ISU international student programs. There are currently 45 Indian students at ISU. The Dases were faculty advisors to the ISU Indian Student Association and helped organize India Night at ISU.

The Dases also participate in community events such as the Portneuf Greenway activities in Pocatello and Heritage and Street Festivals in Idaho Falls, helping to organize Indian food booths. "It is a community service meant to make local people aware of the Indian culture and food," said Nandita.