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Celebrex disrupts heart rhythm in fruit flies

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By Julie Steenhuysen

CHICAGO (Reuters) - Celebrex, an arthritis drug in the same class as the recalled painkiller Vioxx, caused irregular heartbeats in fruit flies and in heart cells taken from laboratory rats, U.S. researchers said on Friday.

"When we tried this drug on the fly heart it became clear that it gave rise to very pronounced arrhythmia," said Dr. Satpal Singh, a pharmacologist at the State University of New York at Buffalo.

"It slows down and becomes irregular," said Singh, whose study appears in the *Journal of Biological Chemistry*.

He found the same effect in heart cells from rats.

Pfizer Inc's Celebrex is one of a class of painkillers that selectively block the COX-2 enzyme, which is involved in inflammation.

COX-2 inhibitors have drawn scrutiny since Merck & Co Inc pulled Vioxx from the market in 2004 after studies showed it raised the risk of heart attacks and stroke in long-term users.

Pfizer pulled a similar drug, Bextra, but has continued to market Celebrex, also known as celecoxib.

What surprised Singh and colleagues was that fruit flies known as *Drosophila* do not have COX-2 enzymes.

They looked further and found that the drug interfered with the passage of potassium in and out of heart cells through pores known as potassium channels.

"We found that one type of channel was very strongly inhibited in its function by the drug," Singh said in a telephone interview. "It is not clear if this channel plays a role in the human heart but it is present," he said.

Pfizer spokesman Jack Cox said while the study is interesting science, "It is important to be cautious about making a leap between this type of information and its effects in people."

"Abnormal heart rhythms and changes in electrocardiograms have been

reported very rarely in clinical trials and in patients with Celebrex as well as with other non-steroidal anti-inflammatories (NSAIDs) such as ibuprofen and naproxen," he said in an e-mail.

"This information is already included in the Celebrex label."

Singh said the research, which was funded by the National Science Foundation, is preliminary and would need to be confirmed in humans.

He said the findings could not be extrapolated to other COX-2 drugs because the effect did not depend on its action on the COX-2 enzyme. "It is a completely unexpected mechanism. It begs for further study," he said.

Pfizer's Cox said the best way to assess the cardiovascular safety of NSAIDs is through a long-term, prospective clinical trial involving thousands of patients, which the company plans to undertake.

COX-2 inhibitors were invented as a safer alternative to aspirin and other NSAIDs, which can cause stomach bleeding.

(Editing by Maggie Fox and Stuart Grudgings)

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