Data from a recent study shows that GlaxoSmithKlines Imitrex® tablets formulated with RT technology™ are absorbed faster than the conventional tablet and disintegrate up to six times faster .

Imitrex® formulated with RT technology™ is absorbed faster than conventional imitrex tablets

Data presented recently at the 47th Annual American Headache Society Scientific Meeting (CA, USA) reported that Imitrex® (sumatriptan succinate) tablets, when formulated with RT technology™, disintegrate up to six times faster and are absorbed more quickly than the conventional tablet.

Data was obtained as a result of a four-way crossover pharmacokinetic trial of five migraine sufferers. The trial compared conventional imitrex (radiolabelled) tablets with the RT technology formulated version. Studies were then made of the gastrointestinal tract using γ-scintigraphy images and end points were recorded as disintegration, gastric emptying and time to onset of absorption.

Results demonstrated that the mean time-to-disintegration for the imitrex tablets formulated with RT technology was six times faster than the conventional tablets, and the mean time to 50% gastric emptying was 30 mins faster. It also showed that at 20 mins, plasma levels with the use of formulated imitrex was five times greater than the conventional tablet.

However, bioequivalency data measured by area under the curve $(AUC)_{0-24}$ and C_{max} demonstrated that formulated imitrex is bioequivalent to conventional imitrex; and therefore the clinical significance of the scinitgraphy findings are inconclusive.

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The study findings were presented by Shashidhar Kori, Director of Clinical Development, Neurosciences Medicine Development Center, North America, GlaxoSmithKline, who commented "We conducted this study to evaluate if the tablet formulated with RT technology could deliver faster disintegration and absorption." Dr Kori continued that "These findings are important because they provide insight into how this delivery technology works in the gastrointestinal tract."

The new formulation of imitrex has been designed to enhance dispersion and dissolution of sumatriptan, the active ingredient of the drug, even when used in the presence of gastric statis, which can delay the disintegration of drugs in the stomach.

Commenting on the study findings, Sheena Aurora, Director if the Swedish Headache Center (WA, USA) noted "In my experience, many migraineurs prefer oral therapy to treat their migraines." However, Sheena Aurora did comment further on the importance of this type of research given that "gastric stasis, a common occurrence in migraine patients, has the potential to limit the efficacy of medicine that is swallowed. Therefore research to identify innovative ways to deliver migraine medication is crucial."

Imitrex was the first triptan to receive US Food and Drug Administration (FDA) approval for the treatment of acute migraine in the adult population and has treated approximately 764 million migraine sufferers over the past decade. However, imitrex is currently contraindicated in patients with certain types of heart disease, history of stroke or transient ischemic attack (TIA), peripheral vascular disease, Raynaud syndrome, or blood pressure that is uncontrolled.

New study findings may lead to better treatment options for patients with schizophrenia

A recent study, carried out by researchers at the McLean Hospital, an affiliate of Harvard Medical School (MN, USA) has, for the first time, found evidence of a direct link between findings observed in the brains of people with schizophrenia following postmortem and electrophysiologic recordings from the brains of rats following experimentally induced simulations.

Francine Benes, Director of the McLean Program in Structural and Molecular Neuroscience, commented on the significance of the findings that "The ability to predictably induce changes in the rat model makes it possible to develop new molecular strategies for the treatment of schizophrenia, ones that are based on specific changes in neural circuitry within the brain."

Researchers at the hospital developed a rat model where they could stimulate increased electrical activity originating in the amygdala and found that this stimulation produced changes in the γ-amino-butyric acid (GABA) cell, which were similar to those seen previously in humans with schizophrenia. The study was published in *Proceedings of the National Academy of Sciences*.

Priority Paper Alerts

Levalbuterol versus racemic albuterol in the treatment of acute exacerbation of asthma in children.

Hardasmalani MD, DeBari V, Bithoney WG, Gold N. *Pediatr. Emerg. Care* 21(7), 415–419 (2005).

This prospective, double-blind, randomized trial was designed to compare levalbuterol and racemic albuterol for the treatment of acute exacerbation of asthma in a pediatric emergency department of an urban tertiary care hospital. Patients (children aged between 5 and 21 years with a history of asthma) received three back to back treatments of either 1.25 mg of levalbuterol or albuterol 2.5 mg via nebulization along with ipratropium hydrochloride every 20 mins with a maximum of three 2 mg/kg doses of oral prednisone administered after the second treatment. All patients showed an improvement in oxygen saturations, respiratory rates and peak flow rates; however, no statistically significant difference was observed regarding the respiratory parameters ($p > 0.05$) and the authors concluded that levalbuterol is not more efficacious than racemic albuterol in improving respiratory parameters in children presenting with acute exacerbation of asthma.

What happens to adverse events during 6 months' treatment with selective serotonin reuptake inhibitors?

Demyttenaere K, Albert A, Mesters P, Dewe W, De Bruyckere K, Sangeleer M. *J. Clin. Psychiatry* 66(7), 859–863 (2005).

A total of 85 psychiatric outpatients with a Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) diagnosis of major depressive disorder were examined in a multicenter randomized, double-blind trial with selective serotonin reuptake inhibitors (fluoxetine [n = 42] and paroxetine [n = 43]) to determine the time course of adverse events during 6 months of antidepressant treatment. Treatment-emergent adverse events were assessed and general linear mixed modeling was used to investigate the predictors of the time course of adverse events. Results showed that the number of at least moderately severe adverse events overall decreased over time, with more severely depressed patients reporting more adverse events than those less severely depressed. The decrease in reported adverse events was comparable over time. Both men and women reported the same number of at least moderately severe adverse events in the first instance, but the habituation was more rapid in men and the authors concluded that the time course of adverse events varies with the severity of depression, sex, completer or dropout status and recurrent versus first-episode depression.

Four of five perinatal strokes lead to neurologic disorders

According to a study published online in the July issue of the *Annals of Neurology*, four out of five newborns who undergo stroke around the time of birth will go on to develop a number of neurologic disorders such as cerebral palsy, epilepsy or language delay.

Senior author of the study and child neurologist at the University of California (SF, USA), Yvonne Wu, commented that "Previous studies suggested that approximately half of all infants with stroke at or near the time of birth have a normal outcome," however, she continued that the current study reports "a higher rate of significant long-term neurologic impairment."

The study is the first of its kind to examine neurologic outcomes following perinatal arterial stroke, including all infants diagnosed within a large population. The study was carried out in collaboration with the Northern California Kaiser Permanente Medical Care Program who examined medical records of over 199,000 children born within the care program between 1997 and 2002.

It was found that the most common disability occurring in perinatal stroke survivors (25%) was cerebral palsy. It was also found that cerebral palsy was more likely to occur in infants who had no other symptoms in early life and it was in such cases that perinatal stroke was discovered in the months following birth when a diminished use of one hand was noted. "Not surprisingly, we found that a larger extent of brain injury, and injury to specific areas of the brain that control movement were both factors that increased the risk of cerebral palsy" said Wu.

However, Wu and colleagues were keen to comment that the "data do not directly impact the current treatment of perinatal stroke," and that the authors did not find any cases of stroke recurrence which strengthens the argument that prophylactic anti-stroke medication should not be administered to such infants.

"However, we hope to raise awareness of this disorder," said Wu. "Infants with unexplained seizures or weakness on one side of the body should be evaluated by a neurologist, and should receive a head imaging study to evaluate for perinatal stroke."

Ranbaxy Laboratories Ltd gain FDA marketing approval for Glimepiride®

Ranbaxy Laboratories Limited have announced that they have received tentative US FDA approval to manufacture and market glimepiride tablets, 1, 2, 4 and 8 mg. The drug is currently indicated as an adjunct to diet and exercise in lowering blood glucose levels in patients with noninsulin-dependent (Type II) diabetes mellitus (NIDDM) in cases where hyperglycemia cannot be adequately controlled by diet and exercise alone.

Jim Meehan, Vice President of Sales and Marketing for Ranbaxy commented "We are pleased to receive this tentative approval for Glimepiride tablets. This product represents an interesting opportunity for Ranbaxy in which we will offer four strengths of this oral hypoglycemic agent to support patient compliance."

Possible link found between the use of opiate drugs and the development of stress-induced anxiety

New results from a study in rats shows a potential link between the use of opiates and the development of stress-induced anxiety, even after ceasing opiate use.

Results from a new study published in the recent issue of the *Journal of Behavioral Neuroscience* has shown that rats exposed to morphine develop more pronounced biologic and behavioral signs of stress-induced anxiety even after being taken off the drug, implying that stress and the use of opiates are connected.

The study could help to explain why opiate users can experience anxiety problems, such as post-traumatic stress disorder, even after they have ceased using the drugs. In such circumstances it is usual for the individual to begin using opiates again as a means of coping with their anxiety disorder. Therefore, it is hoped that a better understanding of how opiate users deal with stress may aid in identifying better treatment options and preventing relapses.

The study, carried out by Gavin McNally and colleagues at the University of New South Wales (NSW, Australia) used rats to measure biologic responses to restraint stress and behaviors that reflect anxiety, such as social interaction and general activity. Results indicated that exposure to morphine left rats more anxious in response to stress, and that the longer the duration or the higher the dose of morphine, the greater the difference in anxiety between morphine- and saline-treated rats. It is speculated by the authors that opitaes may alter the expression of specific anxiety related genes thus priming the nervous system in a lasting way to be more vulnerable to stress.

McNally commented that the exposure to opiates over 5, or fewer days, was not sufficient to alter vulnerability to stress but that "It appears the development of opiate dependence is the critical variable, and there are marked individual differences in humans in the development of dependence. A few days of codeine to relieve post-operative pain are unlikely to lead to the development of dependence."

Autism behaviour types shown to be caused by different sets of genes

A report carried out by researchers at the Medical Research Council (MRC) Social, Genetic and Developmental Psychiatry Centre at the Institute of Psychiatry, King's College London (London, UK) has discovered that two sets of behavior that are required to co-occur for an autism diagnosis, are caused by different sets of genes and are therefore not genetically linked.

The study, which was published in *Developmental Science*, examined data collected from the Twins Early Development Study (TEDS), based in the UK, on 3000 pairs of 7-year old twins through parent and teacher questionnaires which were designed to assess social and non-social behaviors that are characteristic of autism spectrum conditions but also seen in the general population.

For a successful autism diagnosis, two types of behaviors, those reflecting social impairment and non-social obsessive and repetitive behaviors, are necessary. However, it is currently not clear why these two different behavior types co-occur in autism spectrum conditions. Researchers discovered that identical twins generally show either many or few social impairments and fraternal twins can have different levels of social impairment compared with each other. Similar results were found for non-social behaviour disorders thus suggesting that these are both highly heritable.

However, the researchers then investigated whether these different behaviours are influenced by the same set of genes. No evidence was found to indicate that the same genes were involved. The results indicate that the majority of genes that influence social impairments are not the same as those influencing non-social behaviors.

Angelica Ronald of the Institute of Psychiatry, noted that "This study suggests for the first time that social and non-social behaviours, which are both shown in autism spectrum conditions, are caused by mainly different sets of genes. It suggests that 'genes for autism' is a misnomer: there are several genetically distinct components involved. This finding has important implications for DNA and brain studies: it may be better to study the social and non-social components separately rather than requiring that a child has both components, which is what traditional diagnosis requires."

It is hoped that the findings of this study could help in our understanding of autism spectrum disorders and hence contribute towards advancing future diagnosis, and understanding of the condition, eventually leading to a treatment.