ximelagatran for concerns about hepatotoxicity.\cite{14}

**Conclusion**

The novel oral anticoagulant ximelagatran has a favorable pharmacokinetic and dynamic profile as compared to warfarin. It has the potential to initiate the beginning of the end of warfarin. But the propensity to cause hepatotoxicity and the non-availability of an antidote causes concern. So the therapeutic benefits should be weighed against the risks before prescribing it to patients.

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**References**


**Ghrelin: A potential drug target for obesity**

The suffix “ghre” means “to grow”. Ghrelin (pronounced GRELL-in) was discovered in 1999 as a peptide hormone that potently stimulates the release of growth hormone from the anterior pituitary. It was subsequently determined that ghrelin, along with several other hormones, has significant effects on appetite and energy balance.

**Synthesis and receptor**

Ghrelin is synthesized as a pre-prohormone, and then proteolytically processed to yield a 28-amino acid peptide. A modification necessary for biological activity is the binding of n-octanoic acid to one of its amino acids, carried out during its synthesis. Synthesis of ghrelin occurs predominantly in the epithelial cells lining the fundus of the stomach, with smaller amounts produced in the placenta, kidney, pituitary and hypothalamus.

The ghrelin receptor was known well before ghrelin was discovered. Cells within the anterior pituitary have a receptor that, when activated, potently stimulates the secretion of the growth hormone. The receptor was named the growth hormone secretagogue receptor (GHS-R). The natural ligand for the GHS-R is ghrelin. The receptors are present on the cells in the pituitary that secrete the growth hormone and also have been identified in the hypothalamus, heart and adipose tissue.\cite{11}

**Control and physiological effects of ghrelin**

**At least two major biological activities have been ascribed to ghrelin**

1. *Stimulation of growth hormone secretion*: Ghrelin, as the ligand for the growth hormone secretagogue receptor, potently stimulates the secretion of the growth hormone. The ghrelin signal is integrated with that of the growth hormone-releasing hormone and somatostatin to control the timing and magnitude of growth hormone secretion.\cite{2}

2. *Regulation of energy balance*: In rodents and humans, ghrelin functions to increase hunger through its action on the hypothalamic feeding centers. The plasma ghrelin concentrations increase during fasting.\cite{3} Humans injected with ghrelin reported sensations of intense hunger.\cite{4} Ghrelin also appears to suppress fat utilization in the adipose tissue, which is somewhat paradoxical considering that the growth hormone has the opposite effect. Overall, ghrelin seems to be one of
several hormonal signals that communicate the state of energy balance in the body to the brain.

Other effects of ghrelin include stimulation of gastric emptying and a variety of positive effects on cardiovascular function (e.g. increased cardiac output). It is not yet clear whether the cardiovascular effects are due to a direct effect of ghrelin or an indirect effect of ghrelin’s ability to stimulate growth hormone secretion.

**Disease states and ghrelin**

Blood concentrations of ghrelin are lowest shortly after consumption of a meal, and then gradually rise during the fast and reach the peak just prior to the next meal. Ghrelin concentrations in blood are reduced in obese humans compared to lean subjects. However, whether this is the cause or effect is not well defined. Patients with anorexia nervosa have high plasma ghrelin levels whereas obese ones tend to have low levels.

The Prader-Willi syndrome is another disorder relevant to ghrelin. Affected patients develop extreme obesity associated with an uncontrollable and voracious appetite. The plasma ghrelin levels are exceptionally high in comparison to patients similarly obese due to other causes. The Prader-Willi syndrome is clearly a complex disease with many defects. It may be that the excessive ghrelin production contributes to the appetite and obesity components.

**Ghrelin as drug target**

People who lose weight have higher blood levels of ghrelin than they did when they were fat. This also supports the concept that the body tends to maintain its ideal weight and when one loses weight, the body should produce more ghrelin to stimulate to regain the lost weight. Therefore ghrelin makes one fatter by causing hunger to eat more and slowing metabolism to burn fewer calories.

A rise or fall in ghrelin is not observed in patients who had gastric bypass surgery, before or after they eat. Their levels of ghrelin remain low all the time. This shows that stomach cells produce ghrelin only when food passes into the stomach. An empty stomach causes stimulation of ghrelin secretion while food in the stomach stops production of ghrelin. However, when no food enters the stomach for a long time, stomach cells stop producing ghrelin and a person stops being hungry. That is why when it is long past normal mealtime a person stops feeling hungry.

So drugs that can block ghrelin will be very effective to overcome obesity without much disturbance in the physiological homeostasis of our body. Intense research is going on in this regard for a breakthrough drug in obesity.

**References**

5. Weight reduction brought about by caloric restriction caused ghrelin levels to increase, suggesting that ghrelin might contribute to the drive to eat that makes long-term success with dieting so rare. N Engl J Med. 2002 May.