

et la prise en charge des patientes ambulatoires et la mise en place de la recherche sur la pratique pharmaceutique.

Conclusion: Il existe peu de données sur le rôle et les retombées du pharmacien en gynécologie-obstétrique. Le pharmacien en gynécologie-obstétrique de notre centre réalise de nombreuses activités. Nous avons identifié certains éléments à mettre en place pour optimiser la pratique pharmaceutique dans ce secteur.

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Design, synthesis and exploration of structure-function relationship studies of new macrocyclic derivatives of apelin-13

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Introduction: Apelin is the endogenous ligand of the APJ receptor that belongs to class A G protein-coupled receptors. In recent years, the apelin/APJ system has emerged as a promising target for the treatment of various pathophysiological conditions, including regulation of fluid homeostasis, metabolic disorders, and cardiovascular function. We hypothesize that the synthesis of apelin-13 stable analogs may therefore represent a promising avenue for future drug development, notably in the treatment of cardiovascular diseases. Two epitopes seem to play a central role in the biological activity of this peptide. At the N-terminal, the Arg2-Pro3-Arg4-Leu5 moiety is important for binding affinity, while the C-terminal Phe13 of apelin-13 is crucial for receptor internalization as well as hypotensive effects. In an effort to better understand the structure-function relationships of apelin-13, we synthesized a series of macrocyclic analogs of apelin-13 using the “Ring Closing Metathesis” (RCM) method. These analogs were tested for their ability to bind APJ, to inhibit cAMP accumulation, and to induce β -arrestin2 recruitment. The most interesting macrocycles were also assessed in vivo to evaluate their hypotensive effects. The size of the macrocycle between the two epitopes was modified as well as its composition. Our results revealed that keeping the C-terminal amino acid of apelin-13 exocyclic is very important for the binding affinity and signaling. We also discovered several macrocycles possessing an affinity for APJ close to apelin-13 (< 100 nM) that do not activate either cAMP production or β -arrestin2 recruitment. In vivo, after i.v. administration in Sprague-Dawley rats, two macrocycles exhibited a high hypotensive effects. Due to their high stability, these new macrocyclic ligands represent very promising pharmacological tools to better

characterize the signal transduction pathways leading to diverse physiological responses.

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Assessing misclassification in physician-diagnosed diabetes using administrative databases and external validation data

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Objective: We compared the physician-diagnosed diabetes in the Quebec administrative databases with self-reported diabetes and capillary blood glucose levels to estimate the proportion of misclassification of diabetes status in health administrative databases.

Methods: A stratified random sample of 6,247 individuals from was surveyed and asked to provide fasting capillary blood samples. Self-reported diabetes was compared to elevated blood glucose level (2 thresholds were applied: ≥ 7 mmol/L for undiagnosed diabetes; 6.1 - 6.9 mmol/L for prediabetes). A two-stage approach was used to determine the proportion of misclassification. In the first-stage, self-reported diabetes status was corrected for undiagnosed diabetes and prediabetes based on blood results. In the second stage, physician-diagnosed diabetes was compared with self-reported first-stage corrected diabetes status to estimate the proportion of the second-stage misclassification. The proportion of misclassification in the entire random sample was estimated using multiple imputation methodology.

Results: The survey included 3506 participants, among who 1629 provided analyzable blood samples. In the first stage using the capillary blood samples, the proportion of misclassification in self-reported diabetes was 6.6% (95% CI 5.8-7.5%) among survey participants, and in the second stage, the proportion of misclassification in physician-diagnosed diabetes was 11.1% (10.3-11.9%) (2.9% [2.5-3.3%] physician-diagnosed but self-reported nondiabetic and 8.2% [7.5-8.9%] no physician diagnosis but self-reported diabetic). Combining prediabetes and/or undiagnosed diabetes, 21.7% (20.3-23.0%) of the self-reported diabetes was misclassified, and 23.8% (22.8-24.9%) of the physician diagnosis of diabetes was misclassified (2.8% [2.4-3.2%] physician-diagnosed but self-report nondiabetic, 21.0% [20.0-22.1%] no physician diagnosis but self-reported diabetic). For both criteria, the risk of being