CLAIMS

1. Use of an effective amount of a mammalian α-defensin and/or β-defensin selected from the group consisting of hBD-2, HD5, HD6, hBD-1, hBD-3, and hBD-4, in the manufacture of a medicament for the treatment or prevention of a liver, biliary tract, or pancreatic disease or disorder selected from the group consisting of toxic liver disease, alcoholic or non-alcoholic fatty liver disease (NAFLD), liver cirrhosis, hepatic failure, liver fibrosis, liver sclerosis, hepatic encephalopathy, non-alcoholic steatohepatitis (NASH), cholangitis, primary sclerosing cholangitis, cholecystitis and pancreatitis in a subject.

2. The use according to claim 1, wherein the mammalian α-defensin and/or β-defensin comprises a sequence selected from the group consisting of HD5 (SEQ ID NO: 8), HD6 (SEQ ID NO: 9), hBD-1 (SEQ ID NO: 4), hBD-2 (SEQ ID NO: 5), hBD-3 (SEQ ID NO: 6), hBD-4 (SEQ ID NO: 7), and truncated hBD-2 (SEQ ID NO: 17).

3. The use according to any one of the preceding claims, wherein the mammalian α-defensin and/or β-defensin is to be administered at least two to three times a day, such as twice a day, such as three times a day.

4. The use according to any one of the preceding claims, wherein the mammalian α-defensin and/or β-defensin does not further comprise a half-life extending peptide.

5. The use according to any one of the preceding claims, wherein the mammalian α-defensin and/or β-defensin is to be administered to the subject at a daily dosage between 0.1 mg defensin/kg and 10 mg defensin/kg.

6. The use according to any one of claims 1-3 or 5, wherein said mammalian α-defensin and/or β-defensin further comprises at least one further moiety selected from a group consisting of a cell penetrating peptide (CPP), an Albumin Binding Moiety (ABM), a detectable moiety (Z), and a half-life extending peptide.

7. The use of claim 1, wherein the disease or disorder is a liver disorder selected from toxic liver disease, alcoholic or non-alcoholic fatty liver disease (NAFLD), liver cirrhosis, hepatic failure, liver fibrosis, liver sclerosis, hepatic encephalopathy and non-alcoholic steatohepatitis (NASH).

8. The use of any of the preceding claims, wherein the disease or disorder is a liver disease selected from NAFLD and NASH.

9. The use of claim 1, wherein the disease or disorder is a biliary tract disorder selected from cholangitis, primary sclerosing cholangitis and cholecystitis.

10. The use of claim 1, wherein the disease is pancreatitis.

11. The use according to any one of the preceding claims, wherein the subject is an animal.

12. The use according to any one of the preceding claims, comprising at least one mammalian α-defensin and at least one mammalian β–defensin to be administered.

13. The use according to any one of the preceding claims, said use comprising an effective amount of a mammalian α-defensin and/or β-defensin alone or in combination to be administered with antibiotics and/or insulin/insulin analogs and/or glucagon like peptide-1 (GLP-1)/GLP-1 analogs and/or glucagon like peptide-2 (GLP-2)/GLP-2 analogs and/or a dipeptidyl peptidase IV (DPP-IV) inhibitor and/or metformin and/or a sodium glucose transporter-2 (SGLT-2) inhibitor and/or a glucagon receptor antagonist and/or a transient receptor potential cation channel subfamily V member 1 (TRPV1) antagonist to a subject in need thereof.

14. The use according to any one of the preceding claims, wherein the mammalian defensin is HD5 and/or the mammalian defensin is hBD-2.

15. The use according to any one of the preceding claims, wherein the subject has:

a BMI of 25 or more, such as 30 or more, for example 35 or more, such as 40 or more;

a waist/hip ratio of at least 0.80, for example 0.80-0.84, such as at least 0.85 (female) or at least 0.90, for example 0.9-0.99, such as above 1.00 (male);

a fasting blood glucose of at least 6.1 mmol/l, for example at least 7.0 mmol/l; and/or

a glycated haemoglobin level of at least 42 mmol/mol Hb, such as between 42 and 46 mmol/mol Hb, such as at least 48 mmol/mol Hb.

16. The use according to any one of the preceding claims, wherein the subject has one or more of the following symptoms:
    - Elevated blood pressure: ≥ 140/90 mmHg;
    - Dyslipidemia: triglycerides (TG): ≥ 1.695 mmol/L and high-density lipoprotein cholesterol (HDL-C) ≤ 0.9 mmol/L (male), ≤ 1.0 mmol/L (female);
    - AST/ALT > 1;
    - Fasting glucose > 6.1 mmol/L;
    - Central obesity: waist:hip ratio > 0.90 (male); > 0.85 (female), or body mass index > 30 kg/m^2; and
    - Microalbuminuria: urinary albumin excretion ratio ≥ 20 µg/min or albumin:creatinine ratio ≥ 30 mg/g.

17. The use according to claim 6, wherein the half-life extending peptide is selected from a group consisting of a molecule capable of binding to a neonatal Fc receptor (FcRn), transferrin, albumin (HAS), XTEN or PEG, a homo-amino acid polymer (HAP), a proline-alanine-serine polymer (PAS), or an elastin-like peptide (ELP), hyaluronic acid, a negatively charged sialylated peptide such as the carboxy-terminal peptide (CTP) of chorionic gonadotropin (CG) β-chain, human IgG, and CH3(CH2)nCO- wherein n is 8 to 22.

18. The use according to any one of claims 1-2 or claims 4-17, wherein the mammalian α-defensin and/or β-defensin is to be administered to the subject once a day, two times a day, or three times a day.

19. The use according to any one of claims 1-2 or claims 4-18, wherein the mammalian α-defensin and/or β-defensin is to be administered to the subject once, twice or three times a week e.g. every second day.

20. The use according to any one of the preceding claims, wherein the mammalian α-defensin and/or β-defensin is to be administered by addition to a food or a drink.

21. The use according to any one of the preceding claims, wherein the mammalian α-defensin and/or β-defensin is to be administered to the subject is oral or subcutaneous.