Classical treatment of ulcerative colitis is focused on controlling flare-ups and reducing the chances of further flare-ups or complications. For many years, the drug compound Mesalazine (5-amino-2-hydroxy-benzoic acid) was a standard therapy for mild and moderate ulcerative colitis. Mesalazine and the drug compounds Sulfasalazin, Olsalazine, Balsalazine are also together named 5-ASA-compounds. There is however an increasing number of ASA-refractory individuals. Many individuals become 5-ASA-refractory or do not tolerate 5-ASA-compounds, in particular the compound Mesalazine.

Other treatments for ulcerative colitis and flare-ups include steroid therapy, the use of immune-suppressants, the use of TNF-antagonists and/or surgery. Although steroids are often effective at reducing bouts of inflammation, adverse side effects are associated with long term steroid use. ASA-refractory in the context of this invention means that the symptoms of the disease ulcerative colitis are not considerably improved by using the above mentioned 5-ASA-compounds, and in particular 5-amino-2-hydroxy-benzoic acid.

The present disclosure relates to the treatment of ulcerative colitis by using specific formulations of particular phosphatidylcholine products. The disclosure also relates to the new formulations as described in the patent claims.

Phosphatidylcholines are responsible for the establishment of the protective hydrophobic surface, holding a key role in mucosal defence processes. Patients with ulcerative colitis have significantly less phosphatidylcholines in their intestinal mucus compared to Crohn's disease patients and healthy controls. A damaged phosphatidylcholine layer may lead to inflammation and ulceration. Phosphatidylcholines and other lipids were shown in the literature to inhibit pro-inflammatory signal processes and to alleviate inflammatory activity caused by ulcerative colitis. From in vitro and in vivo experiments in mice and rats it can be seen that phosphatidylcholines are actively secreted into the ileum. Phosphatidylcholines are moved continuously from caecum to rectum by colonic activity, the rectum being the last area supplied with phosphatidylcholines.

It is an object of the embodiments disclosed herein to provide new pharmaceutical formulations for ulcerative colitis treatment, in particular for ulcerative colitis treatment in patients that are refractory to classical treatment (such as 5-ASA, steroids or immunesuppressants). These formulations have an improved efficacy and/or less severe consequences or side effects than the limited treatment options with known classical formulations available. Furthermore, side effects (such as flatulence) are observed with a lower frequency.

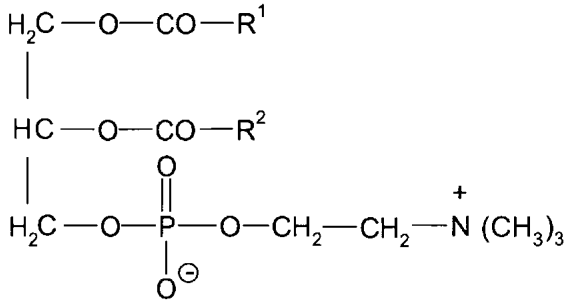
Furthermore, the daily dose of PC in many cases can be kept low, which improves patients' compliance. These formulations often are multiple unit dosage forms which are presented in a single dose container containing the exact amount of formulation for one administration time point, which allows a high uniformity of dosing in contrast to existing formulations which are provided in multi-dose containers and dosed by patients themselves with a measuring cup.

As some individuals have a severe progression of the disease, even with a classical long term steroid and/or 5-ASA treatment, new formulations are also needed to provide better therapy. Other individuals do not favorably respond or become substantially irresponsive to steroid and/or 5-ASA treatment. For individuals having a 5-ASA-refractory disease, a removal of the colon can become necessary.

The present disclosure in particular relates to a pharmaceutical formulation comprising a particular phosphatidylcholine product (PC) for ameliorating at least one symptom of ulcerative colitis. This particular, the phosphatidylcholine product (PC) is combined with specific excipients for a delayed release formulation, often as a multiple unit dosage form, presented in a single dose container.

In an aspect, there is provided a pharmaceutical formulation, comprising:

at least one phosphatidylcholine product (PC) of formula (I),



(I)

wherein:

R^1 is the residue of a saturated or unsaturated fatty acid with 12-24 carbon atoms, and R^2 is the residue of a saturated or unsaturated fatty acid with 12-24 carbon atoms, and wherein the phosphatidylcholine product (PC) contains the following amounts of fatty acids (in weight percent of the total amount of fatty acids in the PC):

55 – 72	linoleic acid
10 – 18	palmitic acid

07 – 15	oleic acid
02 – 08	linolenic acid
02 – 08	stearic acid,

and at least one pharmaceutically acceptable excipient for delayed release of the phosphatidylcholine product (PC),

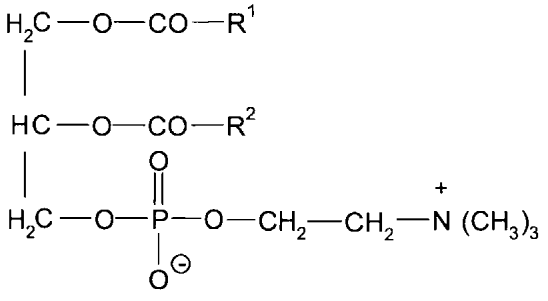
wherein the phosphatidylcholine product (PC) denotes at least 94 % by weight of all lipid/phospholipid components of the formulation.

In an aspect, there is provided a process for the preparation of a pharmaceutical formulation as defined above, comprising the step of preparing pellet(s) or capsule(s) or granule(s) or tablet(s), containing at least one phosphatidylcholine product (PC) of formula (I), and then providing the pellet(s) or capsule(s) or granule(s) or tablet(s) with at least one layer of at least one enteric polymer coating.

In another aspect, there is provided a formulation as defined above for the treatment or prevention of a condition or disease from the following: ulcerative colitis, Crohn's disease, diversion colitis, infectious enteritis, infectious colitis, inflammation due to irradiation and inflammation due to chemotherapeutics or chemicals, in particular for the treatment of ulcerative colitis in 5-ASA-refractory patients.

In one embodiment, the pharmaceutical formulation of the invention comprises:

a) at least one phosphatidylcholine product (PC) of formula (I),



(I)

wherein:

R^1 is the residue of a saturated or unsaturated fatty acid with 12 to 24 carbon atoms, and R^2 is the residue of a saturated or unsaturated fatty acid with 12 to 24 carbon atoms. R^1 and R^2 often are residues of saturated or unsaturated fatty acid with 14 to 22 carbon atoms.

The two fatty acid chains R^1 and R^2 in formula (I) are often not the same. The percentage of unsaturated fatty acid residues for R^1 in one embodiment of the invention is lower than for R^2, e. g. R^1 has less than 70% (by weight) unsaturated fatty acids whereas R^2 has more than 90% unsaturated fatty acids.