INTRODUCTION

Non-specific inflammatory bowel diseases (IBDs), including ulcerative colitis and Crohn’s disease, are chronic non-infectious diseases that showed an increase in prevalence in recent years, particularly in the developed countries. The effective methods of their treatment and prevention of recurrences are currently under investigation. One type of therapy that can prevent the inflammatory recurrence in the gastrointestinal tract is the PPAR-γ agonists thiazolidinediones. Numerous studies available in literature have confirmed the beneficial effects of thiazolidinediones (glitazones), namely rosiglitazone and troglitazone in the gut. The objective of the present study was to compare the possible effects of rosiglitazone 10 mg/kg b.w. or 30 mg/kg b.w. and troglitazone 30 mg/kg b.w. on experimental colitis induced by administration of 1.5% dextran sodium sulphate (DSS) administered in drinking water to rats. Specimens collected from the large intestine were microscopically evaluated, and concentrations of Th1 dependent (IL-2, INF) and Th2 dependent (IL-4, IL-10) cytokines were determined in the serum and intestinal homogenates. Both rosiglitazone and troglitazone have demonstrated significant anti-inflammatory properties. This observation was confirmed by histopathological and immunoenzymatic tests. The therapeutic efficacy of rosiglitazone was dose-dependent. Troglitazone resulted in significantly stronger enhancement of anti-inflammatory cytokine expression than rosiglitazone and comparable down-regulation of pro-inflammatory cytokine expression compared to rosiglitazone used in a higher dose.

Key words: colitis, inflammatory bowel diseases, peroxisome proliferator-activated receptors gamma, rosiglitazone, troglitazone, dextran sodium sulphate
carried out by Celinski et al. (13). In the present study, the model with 1.5% DSS was used.

The aim of the study was to analyse and compare the possible effects of PPAR-γ agonists, rosiglitazone, 10 mg/kg b.w. or 30 mg/kg b.w. and troglitazone 30 mg/kg b.w. on experimental colitis induced with 1.5% DSS administered in drinking water in rats. For complete assessment of their effects, intestinal specimens were macroscopically and concentrations of Th1- and Th2-dependent cytokines (IL-2, IL-4, IL-10, and INF respectively) were determined in the serum and intestinal homogenates.

MATERIAL AND METHODS

Experiments followed the protocol approved by the local Animal Ethics Committee in Lublin (no. 23/2008).

The experiments were carried out in Wistar female rats weighing 200–220 g. Animals were randomly selected and study and control groups were examined simultaneously. Colitis was induced with 1.5% DSS administered in the drinking water ad libitum for 14 days. In various studies available, experimental colitis was induced administering DSS for several to twenty days in the concentrations of 1% to 5%, or even 9% (14-23).

Rosiglitazone, 10 and 30 mg/kg b.w. and troglitazone, 30 mg/kg b.w. were administered 4 times before induction of colitis through a gastric probe. Both rosiglitazone and troglitazone were dissolved in 0.9% NaCl to the volume of 1 ml. Rats were decapitated with a guillotine and blood was sampled for clotting testing; the large intestine was collected, longitudinally sectioned and faecal residues were removed. The specimens for histopathologic evaluation and for enzyme-linked immunosorbent assay (ELISA) were prepared. The specimens for immunoenzymatic testing were homogenized by adding 2 ml of 0.9% NaCl to the volume of 1 ml. Rats were decapitated with a guillotine and blood was sampled for clotting testing; the large intestine was collected, longitudinally sectioned and faecal residues were removed. The specimens for histopathologic evaluation and for enzyme-linked immunosorbent assay (ELISA) were prepared. The specimens for immunoenzymatic testing were homogenized and frozen at –80°C. The levels of cytokines IL-2, IL-4, IL-10 and INF were determined in the intestinal homogenate and serum. The randomization into study groups (8 rats each) and methods of administration of the substances used are presented in Table 1.

Histopathologic evaluation

The collected large intestine was divided into segments: S1 – the rectum up to 2 cm; S2 – from 2 to 5 cm; S3 – from 5 to 10 cm; S4 – from 10 cm to the caecum; S5 – the caecum. From each segment, sections for microscopic evaluation were collected: S1 – the rectum up to 2 cm; S2 – from 2 to 5 cm; S3 – from 5 to 10 cm; S4 – from 10 cm to the caecum; S5 – the caecum. From each segment, sections for microscopic evaluation were collected:

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Substances and routes of administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>8</td>
<td>Control group - access to food and water ad libitum</td>
</tr>
<tr>
<td>B</td>
<td>8</td>
<td>1.5% DSS in drinking water ad libitum for 14 days</td>
</tr>
<tr>
<td>C</td>
<td>8</td>
<td>1.5% DSS in drinking water ad libitum for 14 days and 4 doses of rosiglitazone 10 mg/kg b.w. dissolved through a gastric probe on day 4, 7, 10, 13.</td>
</tr>
<tr>
<td>D</td>
<td>8</td>
<td>1.5% DSS in drinking water ad libitum for 14 days and 4 doses of troglitazone 30 mg/kg b.w. on day 4, 7, 10, 13.</td>
</tr>
<tr>
<td>E</td>
<td>8</td>
<td>1.5% DSS in drinking water ad libitum for 14 days and 4 doses of troglitazone 30 mg/kg b.w. on day 4, 7, 10, 13.</td>
</tr>
<tr>
<td>F</td>
<td>8</td>
<td>4 doses of rosiglitazone 10 mg/kg b.w. on day 1, 3, 5, 7.</td>
</tr>
<tr>
<td>G</td>
<td>8</td>
<td>4 doses of rosiglitazone 30 mg/kg b.w. on day 1, 3, 5, 7.</td>
</tr>
<tr>
<td>H</td>
<td>8</td>
<td>4 doses of troglitazone 30 mg/kg b.w. on day 1, 3, 5, 7.</td>
</tr>
</tbody>
</table>

The histological specimens were evaluated using the light microscope Axioskop plus (ZEISS, Germany).

Enzyme-linked immunosorbent assay (ELISA)

Immediately after decapitation, the blood, about 10 ml, was sampled for clotting testing. After centrifugation at 5000 rpm, the serum was frozen at –80°C. The large intestine parts for immunoenzymatic assay were homogenised by adding 2 ml of phosphate-buffered saline (PBS) without Ca²⁺ and Mg²⁺ ions (Biomed Lublin, Poland). The solution was centrifuged at 2000 rpm, and the supernatant was frozen at –80°C. The concentrations of IL-2, IL-4, IL-10 and INF were determined in the serum and intestinal homogenates. The results were read using the ELISA Victor 3 reader (Perkin Elmer USA). The protein concentrations in the samples tested were calculated with KCJR software.

Statistical analysis

The Kolmogorov-Smirnov, Student’s t, Cochran-Cox and Levene’s tests were used for calculations of descriptive statistics, i.e. a mean, variation and standard deviation (S.D.). The results were quantitative, thus the variables were described using a mean and standard deviation (S.D.) as the numerical data had normal distribution (checked with the Kolmogorov-Smirnov test). The intergroup comparisons of
parameters were carried out (groups A–L) once intergroup variations were checked using the Levene’s test. In cases of equal variations, the Student’s t test was used (“t” denoting the test function); otherwise, the Cochran-Cox test was applied (“C” denoting the test function). The error risk was assumed at 5%, which means that the tested hypothesis was rejected at p<0.05 and the alternative hypothesis was true. The intergroup differences were considered significant at p<0.05; at p<0.01, the differences were more significant whereas at p<0.001 highly significant. The calculations were performed using Statistica 9.0 software.

RESULTS

In the control group, the microscopic picture of the large intestine sections was normal. The architecture and structure of intestinal mucosal crypts were preserved with the proper amount of mucus in the lumen. A few mononuclear cells, mainly lymphocytes, were observed in the lamina propria while fine lymph follicles, typical of the large intestine, were found in the submucosa. The epithelium did not show defects and was covered with the mucous layer. The submucosal, muscular and serosal membranes of the large intestine were normal.

In the study groups receiving rosiglitazone, 10 mg/kg b.w. or 30 mg/kg b.w. and troglitazone 30 mg/kg b.w., the microscopic picture of the large intestine sections was similar to that in the control group. Occasionally, slightly enhanced focal mucosal oedema was observed. The structure of intestinal mucosal crypts was preserved with the proper amount of mucus. Dispersed, fine lymph follicles typical of the large intestine were observed in the lamina propria. The epithelium did not show defects and was covered with the mucus. The submucosal, muscular and serous membranes of the large intestine were normal.

In the group receiving 1.5% DSS, the microscopic picture revealed changes in all segments of the large intestine. Numerous ulcerations and full-wall thickness inflammation of moderate and marked severity, in the form of inflammatory infiltrations consisting of mononuclear cells, such as lymphocytes and plasmocytes (although less abundant), were present in all intestinal segments. The mononuclear cells were observed in the mucosal, submucosal (focally), muscular and serous membranes of the large intestine. The inflammation observed was characterized by substantial activity with the presence of neutrophils. The edema of the mucosa and submucosa was noted in all intestinal segments in all the rats. In the majority of the rats, the mucosal crypts were atrophied in all segments and the amount of mucus in their lumen was reduced.

Five out of eight rats in the group showed ulcerations and erosions of the mucosa were visible in several segments, most pronounced in the distal intestine (S1). In three out of eight rats this group, ulcerations affecting the intestinal lamina propria and muscularis mucosae were observed. In five out of eight rats, ulcerations were focally full-walled involving also the intestinal muscularis mucosae. Focally, the mucosal and submucosal lamina propria at the site of ulcerations was characterized by the presence of slight thickening and slightly marked fibrosis. In all animals receiving 1.5% DSS, dispersed, yet distinct lymph follicles were found in all colon segments; in one animal, they were distinct and numerous.

Both rosiglitazone and troglitazone have been proven to reduce the intensity of the inflammatory infiltration, which was confirmed by histopathological findings. In the groups with 1.5% DSS-induced colitis receiving rosiglitazone and troglitazone, the extent and activity of inflammation were decreased; moreover, the edema and the severity of the ulcerations in the large intestine were significantly diminished. In the group receiving rosiglitazone in a dose of 30 mg/kg b.w. and DSS, the inflammatory features were slightly more suppressed compared to the group administered rosiglitazone in a dose of 10 mg/kg b.w. and DSS. In the former, there were no ulcerations of the mucosa in any intestinal segment, focal crypt atrophy was rarer and the number of mononuclear cells and neutrophilic aggregates lower whereas in the latter, superficial ulcerations of the mucosa were observed in segment S1.

Histopathologically, there were no significant differences in the severity of inflammation in the group receiving 1.5% DSS and troglitazone, 30 mg/kg b.w. vs. the group given 1.5% DSS and rosiglitazone, 30 mg/kg b.w. (Figs. 1-5).

The levels of IL-2, IL-4, IL-10 and INF were determined in the serum and intestinal homogenates using ELISA. The comparison of serum and homogenate concentrations in individual groups was presented as an arithmetic mean and standard deviation (S.D.) in Tables 2 and 3.

The immunoenzymatic analysis of the most important cytokines involved in the pathogenesis of IBD demonstrated that PPAR-γ ligands inhibited the expression of pro-inflammatory factors such as IL-2 and INF. Rosiglitazone has shown to be statistically significant in suppressing the expression of IL-2 and INF in the rat serum and intestinal homogenate. Different doses of rosiglitazone did not result in significant differences. In the study group receiving rosiglitazone in a dose of 10 mg/kg b.w., significantly enhanced expression of IL-4 in serum, and IL-10 in serum and homogenates was noted, compared to the group receiving only DSS (Fig. 6, 7). In the group receiving rosiglitazone in a dose of 30 mg/kg b.w., the effects were more pronounced - increased IL-4 was also observed in the intestinal homogenate. An increase in IL-10 in the serum and intestinal homogenate as well as in IL-4 in the intestinal homogenate was

Fig. 1. Control group. Mucicarmine ×400. Intact intestinal mucosa. In intestinal crypts, the goblet cells and mucus secretion on the top of epithelial cells are clearly visible.
Fig. 2. DSS-induced ulceration and oedema of intestinal mucosa. Numerous neutrophils in inflammatory infiltration and abscesses in crypts of intestinal mucosa are observed, H&E method, magn. ×200.

Fig. 3. Representative graph from the group receiving 1.5% DSS and 4 doses of rosiglitazone 10 mg/kg b.w. Moderate inflammatory infiltration in the mucosa and superficially also in the submucosa consisting of lymphocytes, plasmocytes, and dispersed, sparse neutrophils. Slightly distorted architecture of intestinal glands is presented, H&E method, magn. ×200.

Fig. 4. Representative graph from the group receiving 1.5% DSS and 4 doses of rosiglitazone 30 mg/kg b.w. Epithelial defect and slight inflammatory infiltration in the intestinal mucosa consisting of lymphocytes, plasmocytes and dispersed neutrophils could be seen. Slightly distorted architecture of intestinal glands is presented, H&E method, magn. ×200.
Fig. 5. Representative graph from the group receiving 1.5% DSS and 4 doses of troglitazone administrated at the dose of 30 mg/kg b.w. In the mucosa - slight inflammatory infiltration with mononuclear cells consisting of lymphocytes, plasmocytes and focally dispersed neutrophils could be seen. Focally, slightly distorted architecture of intestinal crypts. Slight mucosal and submucosal oedema. The epithelium covered with the layer of mucus of the mucosa and submucosa is observed.

Table 2. Cross tabulation of descriptive statistics for concentrations of IL-2, IL-4, IL-10 and INF in serum. Results presented as a mean and standard deviation (S.D.). Values are expressed in pg/ml.

<table>
<thead>
<tr>
<th>Group</th>
<th>IL-2 Mean</th>
<th>IL-2 SD</th>
<th>IL-4 Mean</th>
<th>IL-4 SD</th>
<th>IL-10 Mean</th>
<th>IL-10 SD</th>
<th>INF Mean</th>
<th>INF SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>63.0900</td>
<td>6.4253</td>
<td>13.4175</td>
<td>0.960681</td>
<td>13.2700</td>
<td>0.663777</td>
<td>74.1625</td>
<td>8.28439</td>
</tr>
<tr>
<td>B</td>
<td>116.5475</td>
<td>19.5864</td>
<td>17.4375</td>
<td>1.331194</td>
<td>21.50125</td>
<td>2.028859</td>
<td>98.76125</td>
<td>5.75183</td>
</tr>
<tr>
<td>C</td>
<td>85.1250</td>
<td>21.2427</td>
<td>14.13375</td>
<td>1.082839</td>
<td>32.85500</td>
<td>7.2226</td>
<td>85.83500</td>
<td>12.67318</td>
</tr>
<tr>
<td>D</td>
<td>82.1850</td>
<td>13.6693</td>
<td>15.28250</td>
<td>1.078541</td>
<td>36.01500</td>
<td>1.9286</td>
<td>79.10375</td>
<td>6.66546</td>
</tr>
<tr>
<td>E</td>
<td>70.4575</td>
<td>8.874457</td>
<td>18.35625</td>
<td>0.873858</td>
<td>40.98125</td>
<td>4.14579</td>
<td>76.12000</td>
<td>10.31233</td>
</tr>
<tr>
<td>F</td>
<td>56.3700</td>
<td>4.06417</td>
<td>14.36250</td>
<td>0.411296</td>
<td>14.36125</td>
<td>0.411181</td>
<td>76.19625</td>
<td>5.931954</td>
</tr>
<tr>
<td>G</td>
<td>56.9875</td>
<td>4.08158</td>
<td>14.68625</td>
<td>0.546206</td>
<td>15.05375</td>
<td>0.755531</td>
<td>76.28375</td>
<td>2.632505</td>
</tr>
<tr>
<td>H</td>
<td>67.59625</td>
<td>12.33432</td>
<td>13.83000</td>
<td>0.638726</td>
<td>13.72125</td>
<td>0.517782</td>
<td>71.36250</td>
<td>5.087845</td>
</tr>
</tbody>
</table>

1P<0.001; 2P<0.01; 3P<0.05 - statistical significance compared to control group.
4P<0.001; 5P<0.01; 6P<0.05 - statistical significance compared to DSS group.
XP<0.001; YP<0.01; ZP<0.05 - statistical significance compared to rosiglitazone given at the dose of 30 mg/kg b.w. +1.5% DSS group.
SP<0.001; TP<0.01; UP<0.05 - statistical significance compared to troglitazone 30 mg/kg b.w. +1.5% DSS group.

Table 3. Cross tabulation of descriptive statistics for concentrations of IL-2, IL-4, IL-10 and INF in intestinal homogenates. Results presented as a mean and standard deviation (S.D.). Values are expressed in pg/ml.

<table>
<thead>
<tr>
<th>Group</th>
<th>IL-2 Mean</th>
<th>IL-2 SD</th>
<th>IL-4 Mean</th>
<th>IL-4 SD</th>
<th>IL-10 Mean</th>
<th>IL-10 SD</th>
<th>INF Mean</th>
<th>INF SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>14.01133</td>
<td>2.13938</td>
<td>4.77632</td>
<td>0.472611</td>
<td>5.804769</td>
<td>1.02949</td>
<td>37.39362</td>
<td>8.50071</td>
</tr>
<tr>
<td>C</td>
<td>45.13672</td>
<td>10.65975</td>
<td>12.70405</td>
<td>2.903172</td>
<td>12.67390</td>
<td>2.896010</td>
<td>57.48643</td>
<td>13.13172</td>
</tr>
<tr>
<td>E</td>
<td>50.48041</td>
<td>7.86732</td>
<td>18.20362</td>
<td>2.994826</td>
<td>22.96387</td>
<td>3.021103</td>
<td>72.24743</td>
<td>17.33533</td>
</tr>
<tr>
<td>F</td>
<td>35.11597</td>
<td>5.97033</td>
<td>15.82955</td>
<td>2.563143</td>
<td>24.55916</td>
<td>4.50134</td>
<td>42.80649</td>
<td>6.487092</td>
</tr>
<tr>
<td>G</td>
<td>40.96354</td>
<td>6.19911</td>
<td>13.70588</td>
<td>1.281784</td>
<td>19.15137</td>
<td>1.905554</td>
<td>64.32225</td>
<td>12.12543</td>
</tr>
</tbody>
</table>

1P<0.001; 2P<0.01; 3P<0.05 - statistical significance compared to control group.
4P<0.001; 5P<0.01; 6P<0.05 - statistical significance compared to DSS group.
XP<0.001; YP<0.01; ZP<0.05 - statistical significance compared to rosiglitazone given at the dose of 30 mg/kg b.w. +1.5% DSS group.
SP<0.001; TP<0.01; UP<0.05 - statistical significance compared to troglitazone 30 mg/kg b.w. +1.5% DSS group.
significantly higher in the group administered rosiglitazone in a higher dose.

Likewise, in the group receiving troglitazone, the expression of IL-10 in the serum and intestinal homogenate as well as IL-4 in the intestinal homogenate was enhanced as compared to the control group (Figs. 8, 9 and 10) and the group receiving only DSS (a significantly higher increase than in the group receiving rosiglitazone 10 mg/kg b.w. and DSS) (Fig. 11). Moreover, the use of troglitazone was associated with reduced expression of IL-2 in the serum and intestinal homogenate as well as INF in the serum (Fig. 12). Compared to rosiglitazone, troglitazone resulted in stronger IL-2 reduction in the intestinal homogenate and stronger increases in serum IL-4 as well as IL-10 in the serum and intestinal homogenate.
DISCUSSION

The incidence of non-specific inflammatory bowel diseases, including ulcerative colitis and Crohn’s disease, is increasingly high, especially in the developed countries, and they constitute a serious clinical problem. Some new methods of treatment and prevention of recurrences of ulcerative colitis and Crohn’s diseases are under research. Once PPARs-γ were identified and

Fig. 9. Changes in mean serum concentrations of IL-10 detected in groups A, B, C, D, E.

Fig. 10. Changes in the mean concentrations of IL-10 in intestinal homogenates in group A, B, C, D, E.

Fig. 11. Alterations in the mean serum concentrations of INF detected in group A, B, C, D, E.
their role in the course of the inflammatory process explained, some of their ligands were hoped to be effectively used for therapy of non-specific inflammatory bowel diseases. The vast majority of literature studies have confirmed beneficial effects of PPAR-γ agonists on macroscopic and histopathological features of colitis.

The findings described by Sanchez-Hidalgo et al. (25) were similar to our results. In their experimental model of colitis induced with intrarectal TNBS, rosiglitazone in the doses of 4 and 8 mg/kg b.w. was used. The intestinal specimens of animals receiving TNBS demonstrated substantial injuries to the mucosa, epithelial necrosis, focal ulcerations and diffuse infiltration with inflammatory cells. In the group administered rosiglitazone 8 mg/kg b.w., no inflammatory cells were observed in the lamina propria, ulcerations were small, not numerous with features of de-epithelisation, and some parts of the epithelium were intact (25). In another study (26), rosiglitazone was used in the doses of 1 and 5 mg/kg b.w. The beneficial effects of PPAR-γ agonist were noted in the group receiving 5 mg/kg b.w. of rosiglitazone, i.e. substantially reduced inflammatory infiltration and small ulcerations in the healing stage. The potentially therapeutic anti-inflammatory properties of thiazolidinedione drugs were also confirmed by Takaki et al. (27). In their experiment, the inflammation inducing agent was 1% DSS in drinking water and PPAR-γ agonists were pioglitazone and netoglitazone. Their effects were evaluated based on the clinical scale (weight loss, faeces consistency, gastrointestinal bleeding), histology findings (severity and extent of the inflammatory reaction, injuries to intestinal mucosa) and length of the large intestine. The results revealed significant anti-inflammatory action of both substances, particularly of pioglitazone.

Moreover, the effects of troglitazone in the doses of 10 and 100 mg/kg b.w. on experimental colitis induced with 1% DSS administered in drinking water for 8 days were assessed (28). The other substance evaluated was bezafibrate - the PPAR-α agonist. In the groups receiving both bezafibrate and troglitazone, statistically significantly reduced features of intestinal wall injury were observed using the point assessment scale of inflammation severity (29). The highest anti-inflammatory efficacy was found in the group administered troglitazone in a dose of 100 mg/kg b.w.

The results of immunoenzymatic tests in the present study are comparable to those reported by Saubermann et al. (29), who induced colitis with 2.5% DSS in drinking water; the PPAR-γ agonists used were rosiglitazone, pioglitazone and troglitazone. PPARs-γ inhibited colitis reducing the concentrations of pro-inflammatory cytokines TNF-α and INF-γ as well as increasing the concentrations of Th2-dependent anti-inflammatory cytokines IL-10 and IL-4. The authors suggested that activated PPAR-γ limited Th1-dependent processes with the shift of activity towards the stimulation of Th2-dependent processes (29). Our findings were similar, i.e. rosiglitazone and troglitazone reduced the expression of Th1-dependent pro-inflammatory cytokines (IL-2 and INF) and activated the expression of Th2-dependent anti-inflammatory cytokines (IL-4 and IL-10).

Furthermore, the effects of rosiglitazone and troglitazone on the inflammatory reactions were studied by Desreumaux and co-workers (30). The authors evaluated anti-inflammatory properties of PPAR-γ agonists and retinoid X receptor (RXR) agonist, with which PPAR forms a heterodimer necessary for proper functioning. Colitis was induced in mice with intrarectal TNBS. Rosiglitazone and troglitazone had shown statistical significance in reducing TNF-α and IL-1β mRNA expression. The simultaneous use of rosiglitazone and RXR agonist resulted in a higher reduction of mRNA expression of pro-inflammatory cytokines. The results of determinations of these parameters were consistent with macro- and microscopic evaluation (30).

The vast majority of literature reports confirm the beneficial effects of PPAR-γ agonists reducing the macroscopic and histopathological features of colitis. In recent years, the first attempts were undertaken to use PPAR-γ ligands in the treatment of non-specific inflammatory bowel diseases in humans. The results of these trials raise hopes that in the nearest future PPAR-γ ligands will be used for therapy of non-specific inflammatory bowel diseases in clinical practice. The available literature data demonstrate that thiazolidinediones, the substances of potential beneficial anti-inflammatory, antineoplastic and hypoglycaemic properties, can also induce adverse side effects, such as cardiac incidents, liver damage, osteoporosis and weight gain. Such side effects were most commonly observed after long-term use of these drugs for the treatment of type 2 diabetes mellitus. In our experiment, rosiglitazone and troglitazone were administered only 4 times over the period of several days, which was not associated with any of the complications mentioned above. The rats receiving thiazolidinedione derivatives gained weight, yet the values of weight gain were not statistically significant, thus were not included in the results.
CONCLUSIONS
1. Rosiglitazone and troglitazone, PPAR-γ agonists, used in rats with experimentally induced colitis had histopathologically confirmed anti-inflammatory effects. The efficacy of rosiglitazone was dose-dependent and comparable to that of troglitazone.  
2. Rosiglitazone reduced the expression of pro-inflammatory cytokines, IL-2 and INF and enhanced the expression of anti-inflammatory cytokines II-4 and II-10. The higher dose induced stronger effects.  
3. Troglitazone-induced up-regulation of anti-inflammatory cytokine expression was stronger than that of rosiglitazone whereas down-regulation of IL-2 and INF expression was comparable to the higher dose of rosiglitazone.  
4. The results of immunoenzymatic determinations of cytokine levels in individual groups of animals confirm the down-regulating effects of activated PPAR-γ on Th1-dependent processes, with the shift of immune activity towards Th2-dependent processes.  
5. Thiazolidinedione drugs, e.g. rosiglitazone and troglitazone used in our study, are likely to be used for the treatment of non-specific inflammatory bowel diseases in future.

REFERENCES


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