Dextran sulfate sodium – DSS for colitis

Trade name: DSS

Chemical names: Dextran sulfate sodium salt, Dextran sulfate

Catalogue number: DB001

CAS nr: 9011-18-1

9042-14-2

Structure:

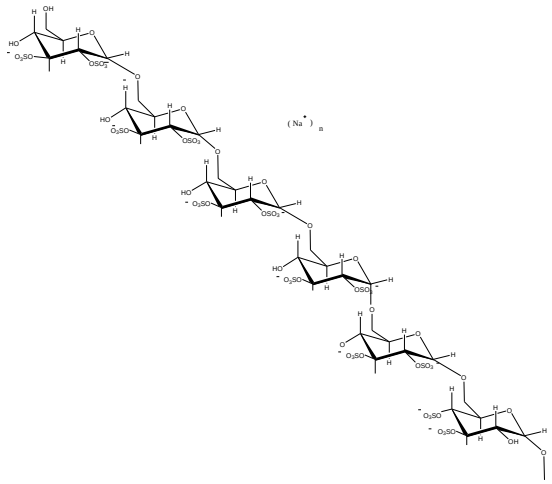

Fig.1. Structural representation of a fragment of dextran sulfate sodium (DSS). Dextran sulfate sodium for colitis has a mean molecular weight of 40 kDa and a sulfur substitution of 1620 %.

What is DSS?

Dextran sulfate sodium abbreviated as DSS is sulfated derivative of a selected dextran fraction. After a program of studies on the various parameters that affect the induction of UC, it was concluded that a dextran fraction with mean molecular weight in the range 40-60 kD and a sulfur substitution of 16-20% gave optimal results.

DSS is a white powder which dissolves freely in water or salt solutions giving a clear solution. The product also dissolves in DMSO, formamide and certain other highly polar organic solvents but is insoluble in lower aliphatic alcohols, acetone, chloroform, dimethylformamide. The pH of an aqueous solution of DSS lies between 6.5 and 7.5. The solution contains a low percentage of phosphate as a stabilizer.

Physical and chemical properties

Molecular weight

The weight average molecular weight (Mw) of DSS lies within the range 35000-55000. A typical distribution is shown in Fig.2. It should be noted that the value for the Mw obtained by gel permeation chromatography (GPC) is a relative value as the column is calibrated with dextran fractions since no standard dextran sulfate fractions are available. Values obtained by light scattering measurements are somewhat lower.

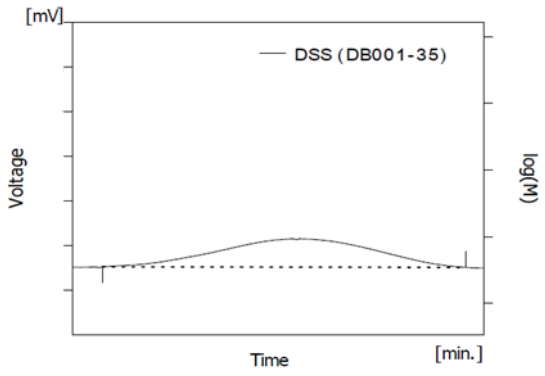

Fig.2 Distribution curve of DSS by GPC

The following factors may contribute to significant deviations in the values obtained by GPC.

1. Choice of column and eluent

2. Flow rate

3. Calibration procedures

4. Deviations in processing chromatograms.

It is therefore crucial that all these parameters be carefully controlled, and the calibration checked continuously against relevant standards.

Sulfation

The degree of sulfation of DSS is also a vital parameter in ensuring potency of the product and should lie between 16 to 20% sulfur.

Generally, this is determined by titration after exchange of the sodium ions. At these levels of substitution, each glucose unit in the dextran chain will contain at least two sulfate groups.

Storage and stability

The stability of dextran sulfate has been studied in both dry form and in solution. In dry form, a retrospective study showed that DSS is stable for more than five years when stored dry in well-sealed containers protected from light at room temperature. Opened containers should be sealed to prevent ingress of moisture.

To study the stability of DSS solutions in water. Solutions of 2.5% DSS were prepared and tested as follows:

1) 2.5% sterile, stored fridge 7 days.

2) 2.5% stored room temp. 11 days.

3) 2.5% stored room temp. 21 days

The results are summarized in Table 1 below.

Sample	Time (days)	pH	Free sulfate (mg/ml)	Mean mol. Wt.	Mw/Mn
1 (control)	7	6.54	0.03	42 000	1.4
2	11	6.25	0.03	41 400	1.4
3	21	5.50	0.03	41 900	1.4

Table 1. *Summary of stability data of dextran sulfate sodium (DSS). DSS was mixed with water to a final concentration of 2.5 %. All reported values are within the expected range. No degradation of DSS was seen during the 21-day study.*

All reported values lie within the expected range and did not provide any evidence of degradation of the DSS solution during the experimental interval studied (max. 21 days).

A prolonged storage (3 months) study of solutions of DSS at room temperature revealed a drop in pH and a slight release of sulfate groups (< 1% of the total). Sterilisation is preferentially performed by sterile filtration.

General notes on the application of DSS

Since its introduction by Okayasu and coworkers in 1987 (1) and subsequent extensive studies on experimentally induced colitis by L-G.Axelsson, A-C.Bylund-Fellenius, S.Ahlstedt and co-workers (2-6), several thousand publications have appeared. The following summary is based on random selection of publications up to 2012 and applications in mice, rats, and other experimental animals. A brief update has been included.

Experimental procedures

Generally, 2-7% solutions of DSS are prepared and filled into the drinking bottles. Although a small percentage of phosphate is added to the DSS during production to stabilize the pH, adjustment 6-7 may be achieved by adding dilute alkali. The solution when not used should be refrigerated. To conserve the amount of DSS used, it is advisable to only fill the bottle with the animals daily requirements. The liquid intake does not appear to be affected by the addition of DSS and free access to 2.5% or 5% DSS represents a daily intake of 3.7 g and 7.4 g per kg per day respectively. (2,p.208).

Dose studies reported by L-G.Axelsson (2) in Balb/c mice receiving 2.5% DSS for up to 35 days did not reveal any mortalities and no rectal bleeding was observed. However, areas of inflammatory activity and significant changes in colon length, spleen weight of feces were noted. At 5% DSS, there was a steady increase in the severity of the inflammation with a pathogenesis resembling human colitis. After day 7, rectal bleeding increased, colon length shortened, and fatalities were recorded. The colitis was most pronounced in the distal colon.

The induction of colitis may be followed by several sets of parameters notably, survival time, body weight, rectal bleeding, spleen weight, diarrhea, colon length and appearance of the intestinal tissue. The symptoms generally appear from 7-10 days. The effect of DSS intake has been related to the actual intake of the solution by the animals. Vowinkel and co-workers used calibrated drinking vessels

for each animal and recorded daily drinking volumes (7). The animals were then grouped according to intake. For practical reasons this procedure is seldom adopted.

DSS in mice

The response to DSS may vary according to the mouse strain used; thus LPS-insensitive strains, C3H//HeJ and C3H/He, showed more severe colitis with inflammatory signs mostly in the proximal colon whereas with BALB/c and CBA/H mice, the inflammatory response was found largely in the distal colon (8). In a further study, mice from nine strains were studied and major differences in genetic susceptibility to DSS were demonstrated (9). The animals received 3.5% DSS in acidified drinking water for 5 days thereafter only water.

In Table 2, data from randomly selected references record the strain/breed of the mice used and the dose and duration in days. Doses have ranged from 1-5% DSS and the duration of treatment from 3 to 35 days. However, in the majority of cases, colitis symptoms appear after 5-7 days (10-35).

Strain	Dose	Reference
Swiss-Webster	(7)	10
TNF-alphaand	-	
TNF-alpha+	4.5% (7)	11
Balb/c	-	12
IL-6and IL-6+	4.5% (8)	13
C57BL/6	2.5%, (5)	14
Wild-type and Fat-1	2.5% (5)	15
Wild-type C57BL/6J(m)	3% (6)	16
C57BL/6 AhR null, WT	3.5% (7)	17
CBA/J(H-2k); BALB/c(H-2d) (f)	5% (7)	18
C57BL/6	5% (3-14)	19
Wild-type; DPIV -/-	2% (6)	20
Mice	3% (7)	21
WTC57BL/6; TR2 KO	3% (7)	22
Balb/c	1% (10)	23
WT C57BL/6(MFG-E8(+)	3.5% (7)	24
WT C57BL/6(IRF4 -/-)	3.5% (5)	25
BALB/c	5% (7)	26
C57BL/6J	3% (5)	27
WT; CCR9(-/-);CCL25(-/-)	2% (7)	28
WT eNOS+/+ and -/-	3%	29
BALB/c; NMRI/KI	2.5 – 5%	30
BALB/c; athymic nu/nu	-	
CD-1(BR)	5% (7-35)	31
IL-5-/and +/+	2.5%, 5% (9)	32
IL-4-/and +/+	-	33
C57BL/6	1.5% (7)	34
BALB/c	15% (10)	35

Table 2. *Treatment of various mice strains with DSS.*

DSS in rats

It has been found that rats generally required a somewhat higher concentration of DSS than mice for inducing experimental colitis. Many studies report the use of 5% DSS solutions. In

Table 3, data from selected references record the strain/breed of the rats used and the dose and duration of treatment (36-46).

Strain	Dose	*Reference*
Wistar	2% (2 weeks-6months)	36
Spraque-Dawley	5% (9)	37
Sprague-Dawley	5% (9)	38
Sprague-Dawley	5% (9)	39
Wistar(4-8week)	2-4% (7)	40
ACI	5 and 10% (14 or 102)	41
Wistar	2.5% (7)	42
Sprague-Dawley	5% (6)	43
Sprague-Dawley (30 day)	0.5-5% (7)	44
Wistar	5% (lowered to 3% (10)	45
Sprague-Dawley	5% (7)	46

Table 3. treatment of various rat strains with DSS. The data comes from selected refeceres

DSS in other animals

Table 4 lists some examples of the use of DSS in other animals.

Strain	Dose	Reference
Hamsters	1% (100)	47
Hamsters	2.5% (6); 3-5% (6)	48
Guinea pig	3% (4)	49
Guinea pig	-	50
Pigs (Yorkshire)	1.25 g/kg BW (5)	51
Pigs	-	52
Pigs	-	53
Pigs	-	54

Table 4. Treatment of other animals with DSS (47-54)

Some consideration should be made when adding other compounds to the DSS solution. DSS is a polyanion and the sulfate groups confer a considerable negative change to the molecule. Thus, addition of compounds with a cationic

character may lead to interactions with the DSS. Since the DSS model has been used to study various therapeutic approaches to the treatment of UC, it would be meaningful to take this into consideration. However, compounds such as sulphasalazine and 5-aminosalicylic acid have not been found to interact (3).

Literature update

Since this file was completed in 2013, interest in the DSS model for studying inflammatory bowel disease (IBD) has continued to grow. Annual statistics for publications involving the DSS model are listed below.

Year	No. of publications
2016	291*
2015	330
2014	270
2013	248
2017	406
2018	476

* Up to August

Most commonly, the model is used to study the mechanisms involved in the development of colitis and other IBDs and particularly the protective immune pathways and how they can be inhibited or stimulated. The therapeutic effects of various chemical agents and cell preparations have also been widely explored. The DSS model has also been valuable in conjunction with azoxymethane treatment or studying the genetic and environmental factors governing colitis associated carcinoma. (68)

Studies using this model have examined many mediators involved in systemic inflammation:

RAMP1, a protein that takes part in the terminal glycosylation, maturation, and presentation of the CGRP receptor to the cell surface (56)

Interleukins (IL-22, IL-23, IL23R, IL12RB1)

which play a vital role in inflammatory processes (55,62,63,66,70)

MMPs (Matrix metalloproteinase) MMP-3-an enzyme that hydrolyzes components of the extracellular matrix e.g., collagen and fibronectin. (64,72,73)

TNF- α ; Tumor necrosis factor is a cytokine involved in systemic inflammation and is a member of a group of cytokines that all stimulate the acute phase reaction (71,74,75)

DOK-1 and DOK-2;. The DOK proteins present a docking platform for the compilation of multi molecular signaling complexes (66)

Remedial effects of stem cells and routes of delivery using the DSS model have been reported (58). Many studies have aimed at evaluating potential therapeutic agents for IBD (59,60,61,66,71,75,76).

The most frequently used strains of mice are C57BL/6, WT or Balb/c but often genetically modified variants have also been used. Doses often depend on the aim of the study and DSS concentrations of 1% are given for mild inflammation thereafter 2-5% for more severe manifestation).

4.2 Reviews

A search for reviews on the DSS model reveals 30 articles since 1987, many of which are directed on selected signaling and receptor processes.

Several reviews appear to be of a more general character (77-81).

References

1. T.Ohkasu, M.Yamada, I.Okayasu et al. Protective effect of metronidazole in experimental ulcerative colitis induced by dextran sulfate sodium. Jpn J Gastroenterolog., 1987;84(10):2337-2346.
2. A-C.Bylund-Fellenius, E.Landström, L-G.Axelsson and T.Midtveldt. Experimental colitis induced by dextran sulfate in normal and germfree mice. Microbial Ecology in Health and Disease. 1994;7:207-215.
3. A-C.Bylund-Fellenius, L-G.Axelsson and E.Land ström. Protective effect of sulfasalazine and olsalazine in dextran sulfate-induced colitis in the mouse. Gastroenterology. 1992;102(4):A600.
4. L-G.Axelsson, E.Landström and A-C.BylundFellenius. Experimental colitis induced by dextran sulfate in mice. Beneficial effects of sulphasalazine and olsalazine. Aliment Pharmacol Ther.1998;12(9):925-34.
5. L-G.Axelsson, E.Landström, A-C.Bylund-Fellenius. Effects of sulfasalazine on survival of athymic mice with dextran sulfate induced colitis. Gut.1992; suppl.33:539.
6. L-G.Axelsson, E.Landström et al. Dextran sulfate sodium (DSS) induced experimental colitis in immunodeficient mice. Effects of CD4+-cell depleted, athymic and NK-cell depleted SCID mice. Inflamm Res.1996;45(4):181-191.
7. T.Vowinkel, TJ.Kalogeris, M.Mori et al. Impact of dextran sulfate load on the severity of inflammation in experimental colitis. Dig Diseases and Sciences. 2004;49(4):556-564.
8. L.Stevceva, P.Pavli, G.Buffinton et al. Dextran sodium sulfate-induced colitis activity varies with mouse strain but develops in lipopolysaccharideunresponsive mice. J Gastroent and Hepatol. 1999;14: 54-60.
9. M.Mähler, I.J.Bristol, E.H.Leiter et al. Differential susceptibility of inbred mouse strains to dextran sulfate sodium-induced colitis, Am J Physiol .Gastrointest Liver Physio., 1998;274: 54-551.
10. H.S.Cooper, S.N.S.Murthy, R.S.Shah, et al. Clinicopathologic study of dextran sulfate sodium experimental murine colitis. Lab Invest. 1993;69(2):238-24.
11. Y.Natio,T.Takagi, O.Handa et al. Enhanced intestinal inflammation induced by dextran sulfate sodium in tumor necrosis factor-alpha deficient mice. J.Gastroenterol.Hepatol. 2003;18(5):560-9.
12. Y.Naito,T.Takagi,T.Ishikawa et al. Alpha-pheny-N-tert-butylnitrone provides protection from dextran sulfate sodium-induced colitis in mice. Antioxid Redox signal. 2002;4(1):195-206.
13. 13.Y.Naito,T.Takagi, K.Uchiyama et al. Reduced intestinal inflammation induced by dextran sulfate sodium in interleukin-6deficient mice. Int J Mol Med. 2004;14(2):191-6.
14. Q.Jia, I.Ivanov, Z.Zlatev, et al. Dietary fish oil and curcumin combine to modulate colonic cytokinetics and gene expression in dextran sulfate sodium treated mice. Brit J Nutr. 2011;106(4):519-9.

15. 15.J.M.Monk, O.Jia, E.Callaway et al. Th 17 Cell accumulation is decreased during chronic experimental colitis by (n-3) PUFA. J Nutr. 2012;142(1):117-24.
16. 16.A.L.Thiess, H.Laroui, T.S.Obertone et al. Nanoparticlebased therapeutic delivery of prohibitin to the colonic epithelial cells ameliorates acute murine colitis. Inflamm. Bowel Dis. 2011;17(5), 1163-76.
17. 17.R.Arsenescu, V.Arsenescu, J.Zhong et al. Role of xenobiotic receptor in inflammatory bowel disease. Inflamm Bowel Dis. 2011;17(5):1149-2.
18. 18.I.Okayasu, S.Hatakeyama, M.Yamada et al. A novel method in the induction of reliable experimental acute and chronic ulcerative colitis in mice. Gastroenterology. 1990;98,:694-702.
19. 19.N.A.Nagalingham, J.Y.Kao, and V.B.Young. Microbial ecology of the murine gut associated with the development of dextran sulfate sodium induced colitis. Inflamm Bowel Disease. 2011;7(4),:917-26.
20. 20.R.Yazbeck, G.S.Howard, R.N.Butler et al. Biochemical and histological changes in the small intestine of mice with dextran sulfate sodium induced colitis. J Cell Physiol. 2011;226(12):319-24.
21. 21.S.Saksena, S.Goyal, G.Raheja et al. Upregulation of P-glycoprotein by probiotics in intestinal epithelial cells and in the dextran sulfate sodium model of colitis in mice. Am J Physiol Liver Physiol. 2011;300(6):G1115-23.
22. 22.W.K.Kim, J.S.Park, O.J.Sul, et al. Role of TNFR-related mediated immune responses in dextran sulfate sodium induced inflammatory bowel disease Mol Cells. 2011;21(2):99-104.
23. 23.R.Palffy, R.Gardlik, M.Behuliak et al. Salmonella-mediated gene therapy in experimental colitis in mice. Ex Biol Med. 2011;236(2):177-83.
24. 24.A.Chogle, H.F.Bu, X.Wang et al. Milk fat globule-EGF factor 8 is a critical protein for healing of dextran sulfate sodium induced colitis in mice. Mol Med. 2011;17(5-6):502-7.
25. 25.J.Mudter, J.Yu, C.Zufferey et al. IRF4 regulates IL-17A promotor activity and controls ROR t-dependent Th 17 colitis in vivo. Inflamm Bowel Dis. 2011;16(6):1343-58.
26. 26.G.K.Kumar, R.Dhamotharan, N.M.Kulkarni. Dextran sulfate sodium induced colitis in mice. Int Immunopharmacol. 2011 Jun;11(6):724-31. doi: 10.1016/j. intimp.2011.01.022.
27. 27.Y.Shiomi, S.Nishiumi, M.Ooi et al. GCMS-based metabolomic study in mice with colitis induced by dextran sulfate sodium. Inflamm Bowel Dis. 2011;17(11):2261-74.
28. 28.M.A.Wurbel, M.G.McIntyre, O.Dwyer, et al. CC125/ CCR9 interactions regulate large intestinal inflammation in a murine model of acute colitis. PLoS One. 2011;6(1):e16442.
29. 29.M.Sasaki, S.Bharwani, P.Jordan et al. Increased disease activity in eNOS-deficient mice in experimental colitis. Free Radic Biol Med. 2003;35(12):1697-87.
30. 30.A-C.Bylund-Fellenius, E.Landström, L.G.Axelsson et al. Experimental colitis induced by dextran sulfate in normal and germfree mice. Microbial Ecology in Health and Disease. 1994;7:207-215.
31. L.G.Axelsson, E.Landström, A-CBylund-Fellenius. Experimental colitis induced by dextran sulfate sodium in mice: Beneficial effects of sulphasalazine and olsalazine. Aliment Pharmacol Ther.1998;12(9):925-34.
32. L.Stevceva, P.Pavli, A.Husband et al. Eosinophilia is attenuated in experimental colitis induced in IL-5 deficient mice. Genes Immun, 2000;1(3):213-8.
33. L.Stevceva, P.Pavli, A.Husband et al. Dextran sulphate sodium-induced colitis is ameliorated in interleukin4 deficient mice. Genes Immun. 2000;2(6):309-16.
34. J.Ramakers, M.I.Verstege, G.Thuijils et al. The PPAR agonist Rosiglitazone impairs colonic inflammation in mice with experimental colitis. J Clin Immun. 2007;27(3):275-283.

35. T.Rochat, L.Bermudez-Humaran, J.J.Gratadoux et al. Anti-inflammatory effects of Lactobacillus casei BL23 producing or not a manganese-dependent catalase on DSS-induced colitis in mice. Micro Cell Fact. 2007;20(6):22.
36. T.Tamaru, H.Kobayashi, S.Kishimoto et al. Histochemical study of colonic cancer in experimental colitis in rats. Dig Dis Sci. 1993;38:529-537.
37. J.Petersson, O.Schreiber ,A.Steege et al. eNOS involved in colitis-induced mucosal blood flow increase. Am J Physiol Gastrointest Liver. 2007;293:G1281-1287.
38. O.Schreiber, J.Petersson, P.Phillipson et al., Lactobacillus reuteri prevents colitis by reducing P-selectin associated leukocyte and platelet-endothelial cells. Am J Physiol Gastrointest Liver. 2009;296:G534-542.
39. J.Dicksved, O.Schreiber, B.Willing et al. Lactobacillus reuteri maintains a functional mucosal barrier during DSS treatment despite mucus layer dysfunction. PLoS One. 2012;7(9):46399.
40. T.Shimizu, M.Suzuki, J.Fujimura et al. The relationship between the concentration of dextran sodium sulfate and the degree of induced experimental colitis in weanling rats. J Pediatric Gastro Nutritio., 2003;37:481486.
41. I.Hirono, K.Kuhara, S.Hoak et al. Induction of intestinal tumors in rats by dextran sulfate sodium. J Natl Cancer Inst. 1981;66(3):579-583.
42. Y.Aoi, S.Terashima, M.Ogura et al. Roles of nitric oxide (NO) and NO synthases in healing of dextran sulfate sodium-induced rat colitis. J Physio Pharmacol. 2008;59(2):315-36.
43. V.Vasina, M.Broccoli, M.G.Ursino et al. Non-peptidyl low molecular weight radical scavenger IAC attenuates DSS-induced colitis in rats. World J.Gastroenterol. 2010;16(29):3642-50.
44. 44 .M.Vicario, M.Crespi, A.Franch et al. Induction of colitis in young rats by dextran sulfate sodium. Digestive diseases and Science, 2005;50(1):143-150.
45. R.Lopez-Posadeas, P.Requena, R.Gonzalez et al. Bovine glucomacropeptide has intestinal anti-inflammatory effects in rats with dextran-sulfate induced colitis. J Nutr. 2010;140(11):2014-19.
46. X.Z.Shi, J.H.Winston, S.K.Sama. Differential immune and genetic responses in rat models of Chron´s colitis and ulcerative colitis. Am J Physiol Gastrointest Liver Physiol. 2011;300(1):G41-51.
47. M.Yamada,T.Ohkusa and I.Ohkusa. Occurrence of dysplasia and adenocarcinoma after experimental ulcerative colitis in hamsters induced by dextran sodium sulfate. Gut. 1992;33:1521-1527.
48. A.Karlsson, A.Jägervall, M.Pettersson et al. Dextran sulfate sodium induces acute colitis and alters hepatic function in hamsters. Int Immunopharmacol. 2008;8(1):20-27.
49. T.Iwanaga, O.Hoshi, H.Han et al. Morphological analysis of acute ulcerous colitis experimentally induced by dextran sulfate sodium in the guinea pig. J Gastrenterol. 1994;430-438.
50. O.Hoshi,T.Iwanaga and M.A.Fujino. Selective uptake of intraluminal dextran sulfate sodium and senna by macrophages in the cecal mucosa of the guinea pig attenuates local inflammation and restores gut homeostasis in a porcine model of colitis. Biochim Biophys Acta. 2009;1790(10):1161-9.
51. D.Young, M,Ibuki,T.Nakamori et al. Soy-derived di-and tripeptides alleviate colon and ileum inflammation in pigs with dextran sodium sulfate-induced colitis. J Nutr. 2012;142(2):363-8
52. C.J.Kim, J.Kovacs-Nolan, C.Yang et al. L-cysteine supplementation attenuates local inflammation and restores gut homeostasis in a porcine model of colitis. Biochim Biophys Acta. 2009;1790(10):1161-9.
53. C.J.Kim, J.Kovacs-Nolan, C.Yang et al. l-Tryptophan exhibits therapeutic function in a porcine model of dextran sodium sulfate (DSS)induced colitis. J Nutr Biochem. 2010;21(6):468-75.

54. M.Lee, J.Kovacs-Nolan, C.Yang et al. Hen egg lysozyme attenuates inflammation and modulates local gene expression in a porcine model of dextran sodium colitis. J Agric Food Chem. 2009;57(6):22332240.
55. K.Aden, A.Rehman, M.Falk-Pauelsen et al. Epithelial IL-23R Signaling licenses protective IL-22 responses in intestinal inflammation. Cell Rep. 2016 Aug 10.pii: S2211-147(16)30985-8.doi:10.1016/j.cel-rep.2016.07.054. (Epub ahead of print)
56. N.Kawashima, Y.Ito, N.Nishizawa et al. RAMP1 suppresses mucosal injury from dextran sodium sulfate-induced colitis in mice. J Gastroenterol Hepatol. 2016 Aug 11. doi:101111/jgh13505 (Epub ahead of print).
57. A.V.Zhdanov, I.A.Okkelman, A.V.Golubeva. Quantitative analysis of mucosal oxygenation using ex vivo imaging of healthy and inflammed mammalian colon tissue. Cell Mol Life Sci. 2016 Aug 10. (Epub ahead of print).
58. E.Legati, M.G.Roubelakis, G.E.Theodoropoulos et al. Therapeutic potential of secreted molecules derived from human amniotic fluid mesenchymal stem/ stroma cells in a mice model of Colitis. Stem Cell Rev. 2016 Aug 8. (Epub ahead of print)
59. A.Wagnerova, J.Babickova, R.Liptak et al. Beneficial effects of live and dead Salmonella-based vector strain on the course of colitis in mice. Lett Appll Microbiol. 2016 Aug 8. Doi:10.1111/lam.12632.(Epub ahead of print)
60. P.Saha, V.Singh, X.Xiao et al. Data on importance of hematopoietic cell derived Lipocalin 2 against gut inflammation. Data Brief. 2016 Jul 2;8:812-6.
61. G.Li, J.Ren, Y.Deng et al. Oral pirfenidone protects against fibrosis by inhibiting fibroblast proliferation and TGF- β signalling in a murine colitis model. Biochem Pharmacol. 2016 Aug 4. pii:S0006-2952(16)30219-2. doi: 10.1016/j.bcp.2016 Aug 8;22:2785-92.
62. J.Yang and L.Xu, Elevated IL-23R Expression and Foxp3+Rorgt+Cells in intestinal mucosa during acute and chronic colitis, Med Sci Monit. 2016 Aug 8;22:2785-92.
63. F.Bootz, B.Ziffels and D.Neri. Antibody-based targeted delivery of interleukin-22 promotes rapid clinical recovery in mice with DSS-induced colitis. Inflamm Bowel Dis. 2016 Aug 1.(Epub ahead of print)
64. M.Chen, L.Gao, P.Chen et al. Serotonin-exacerbated DSS-Induced colitis is associated with increase in MMP-3 and MMP-9 expression in the mouse colon. Mediators Inflamm. 2016;5359768. doi:101155/2016/5359768. Epub 2016 Jul 5.
65. C.C.Wong, L.Zhang, W.K.Wu et al. Cathedin-encoding Lactococcus lactis promotes mucosal repair in murine eperimental colitis. J Gastroenterol Hepatol. 2016 Jul 28, doi: 10.1111/jph.13499
66. M.Waseda, S.Arimura, E.Shimura et al. Loss of Dok-1 and Dok-2 in mice causes severe experimental colitis accompanied by reduced expression of IL-17
67. A and IL-22. Biochem Biophys Res Commun. 2016 Sep 9;478(1)135-42.
68. Z.S.Zádori, V.E.Tóth, A.Fehér et al. Inhibition of a 2A-adrenoceptors ameliorates dextran sulfate sodium-induced acute intestinal Inflammation in mice, J Pharmacol Exp Ther. 2016 Sep;358(3):483-491
69. B.Parang, C.W.Barrett and C.S.Williams, AOM/DSS model of colitis-associated cancer. Methods Mol Biol. 2016;1422:297-307.
70. M.Wang, C.Liang, H.Hu et al. Intraperitoneal injection (IP), Intravenous injection (IV) or anal injection (AI) best way for mesenchymal stem cells transplantation for colitis. Sci Rep. 2016 Aug 4;6::30696. doi:10:1038/srep30696

71. F.Bootz, B.Ziffels and D.Neri. Antibody-based targeted delivery of interleukin-22 promotes rapid clinical recovery in mice with DSS-induced colitis. Inflamm Bowel Dis. 2016 Aug 1. (Epub ahead of print)
72. M.dePaul-Silva, B.E.Barios, L.Maccio-Maretto et al. Role of the protein annexin A1 on the efficacy of anti-TNF treatment in a murine model of acute colitis. Biochem Pharmacol. 2016 Sep 1;115:104-113
73. C.Breynaert, M.de Bruyn, I.Arijs et al. Genetic deletion of tissue inhibitor of metalloproteinase -1/ TIMP-1 alters inflammation and attenuates fibrosis in DSS-induced murine models of colitis. J.Crohns Colitis. 2016 May 17; Pii:jjw 101(Epub ahead of print)
74. P.Niighot, R.Al Sadi, M.Rawat et al. Matrix metalloproteinase 9-induced increase in epithelial tight junction permeability contributes to the severity of experimental DSS colitis. Am J Physiol Gastrointest Liver Physiol. 2015 Dec 15; 309(12):G988-97.
75. B.Aydin, Y.Songur, N.Songur et al. Investigation of pulmonary involvement in inflammatory bowel disease in experimental model of colitis. Korean J Intern Med. 2016Aug 19 doi; 10.3904/kjim.2014.238. (Epub ahead of print)
76. 75 H.Zbakh, E.Talero, J.Avila et al. The Algal Meroterpene 11-hydroxy-1´-O-methylamentadione ameloriates dextran sulfate sodium-induced colitis in mice. Mar Drugs. 2016 Aug 5;14(8). pii: E149. doi: 10.3390/ md14080149.
77. A.Pukhalsky, G.Shmarina, V.Alioshkin et al. Alkylating drugs applied in non-cytotoxic doses as novel compounds targeting inflammatory signal pathway. Biochem Pharmacol. 2006 Nov 30;72((11):1432-8.
78. P.K.Randhawa, K.Singh, N.Singh et al. A review on chemical induced inflammatory bowel disease models in rodents. Korean J Physiol Pharmacol. 2014 Aug;18(4):279-88.
79. S.Sebastian, V.Hernanez, P.Myrled et al., Colorectal cancer in inflammatory bowel disease; results of the 3rd ECCO pathogenesis scientific workshop. J .Crohns Colitis. 2014 Jan;8(1):5-18
80. M.L.Clapper, H.S.Cooper and W.C.Chang. Dextran sulfate sodium induced colitis-associated neoplasmia; a promising model for the development of chemopreventive interventions. Acta Pharmacol Sin. 2007 Sep;28(9):1450-9.
81. G.Rogler and T.Andus. Cytokines in inflammatory bowel disease. World J Surg. 1998 Apr;22(4):382-9.
82. T.Ishicka, N.Kuwwabara, Y.Ochashi et al. Crit Rev Toxicol. 1987; 17(3):215-44.
83. Hoffmann M et al. A refined and translationally relevant model of chronic DSS colitis in BALB/c mice (2018) Lab Anim. 2018 Jun;52(3):240-252
84. Chassaing B et al. Dextran sulfate sodium (DSS)-induced colitis in mice. Curr Protoc Immunol. (2014) Feb 4;104.
85. Li M et al. Initial gut microbiota structure affects sensitivity to DSS-induced colitis in a mouse model. Sci China Life Sci. (2018) Jul;61(7):762-76.