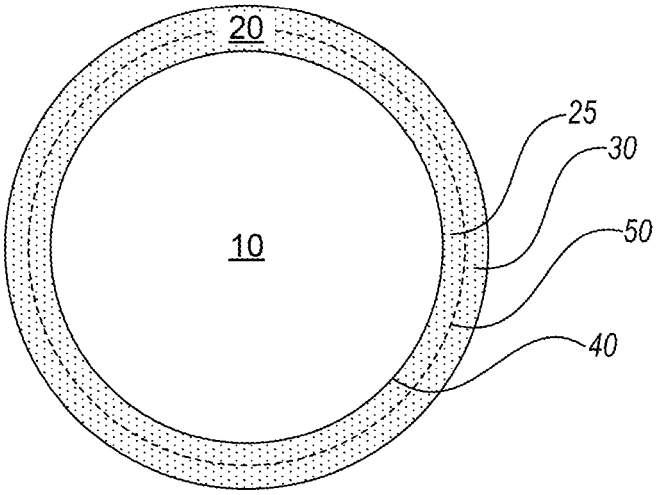

20
25
30
50
10
40

FIG. 1

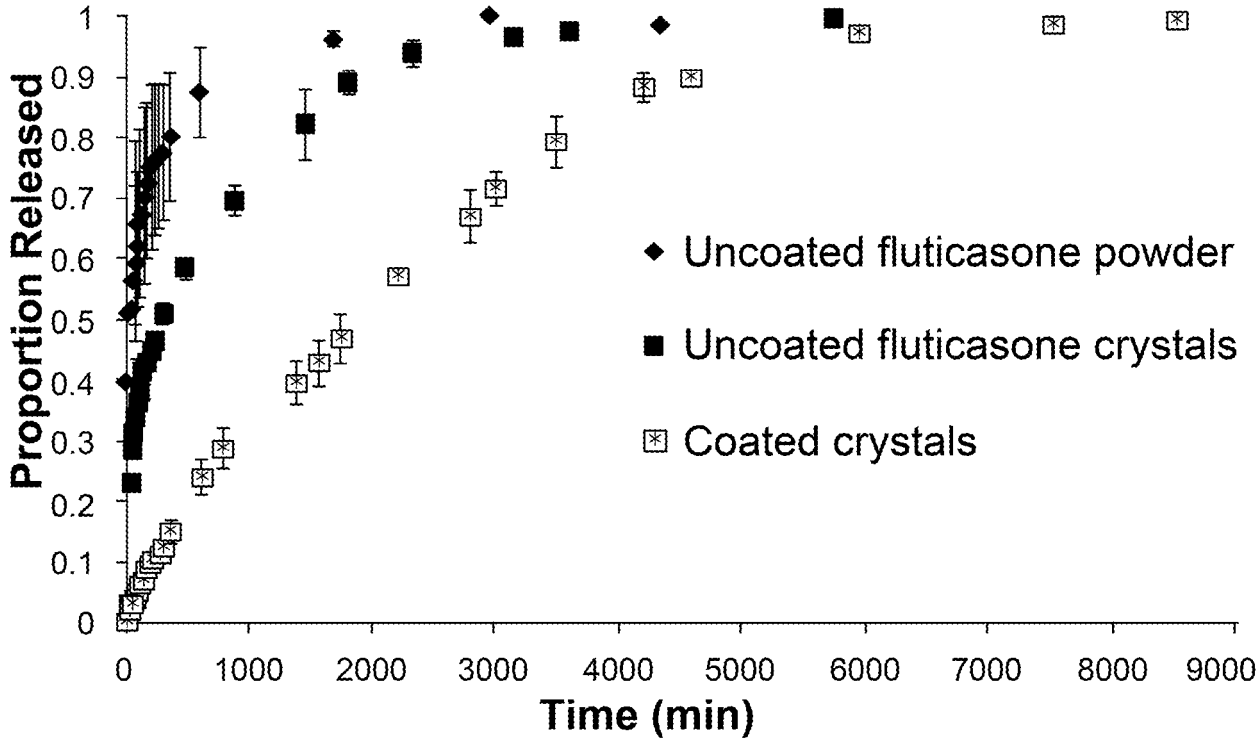

Proportion Released
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
1000
2000
3000
4000
5000
6000
7000
8000
9000
Time (min)
Uncoated fluticasone powder
Uncoated fluticasone crystals
Coated crystals

FIG. 2

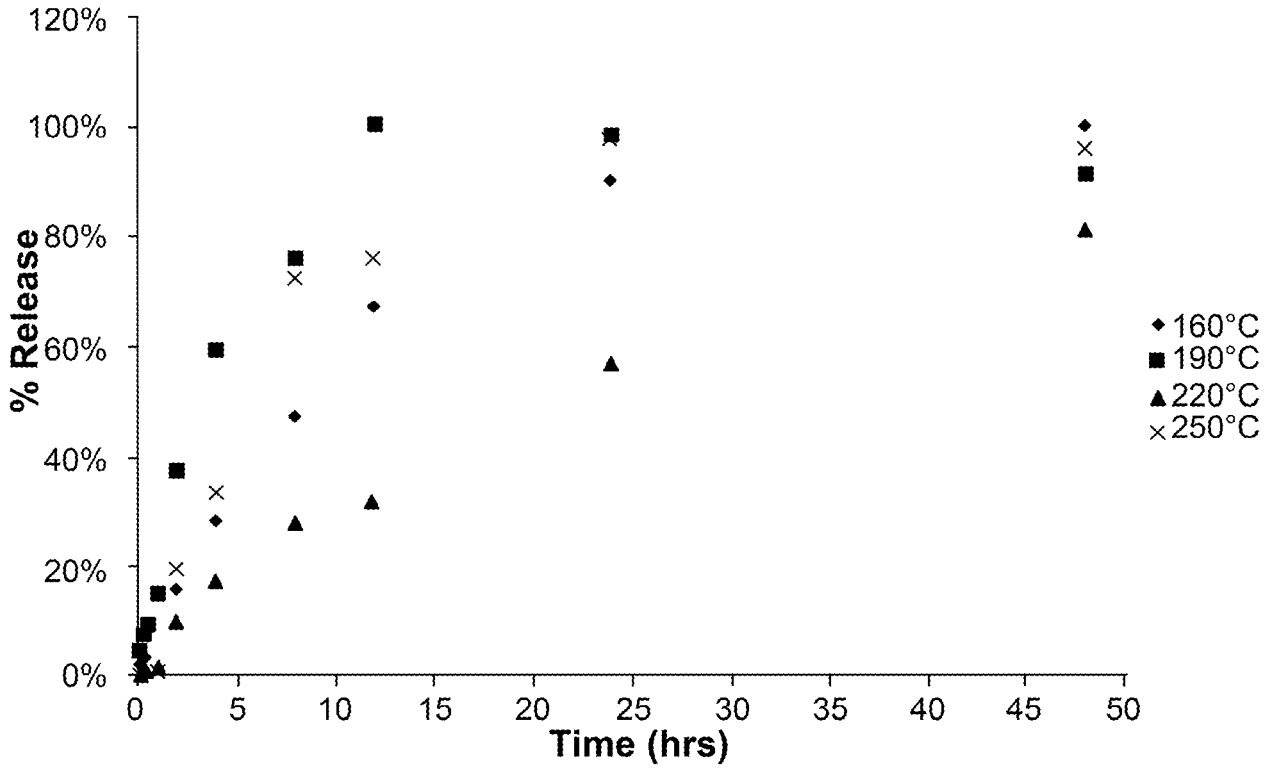

120%
100%
80%
60%
40%
20%
0%
% Release
0
5
10
15
20
25
30
35
40
45
50
Time (hrs)
160°C
190°C
220°C
250°C

FIG. 3A

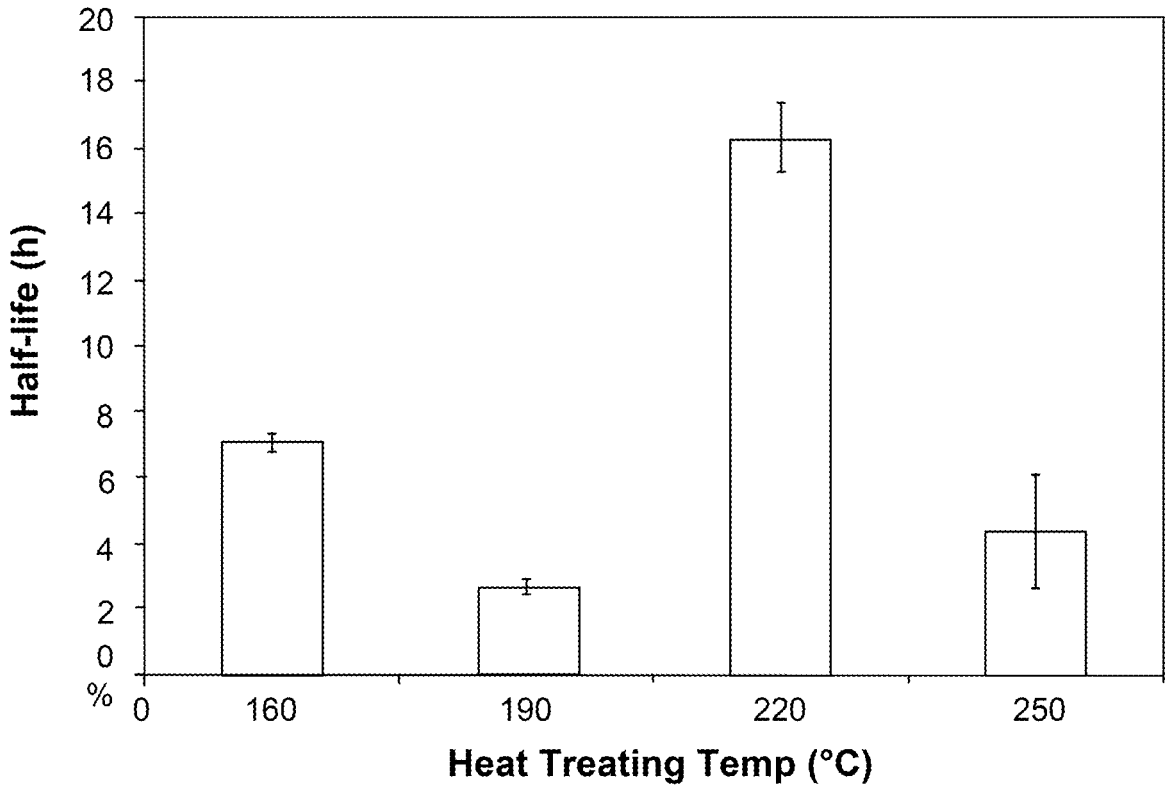

20
18
16
14
12
10
8
6
4
2
0
%
Half-life (h)
0
160
190
220
250
Heat Treating Temp (°C)

FIG. 3B

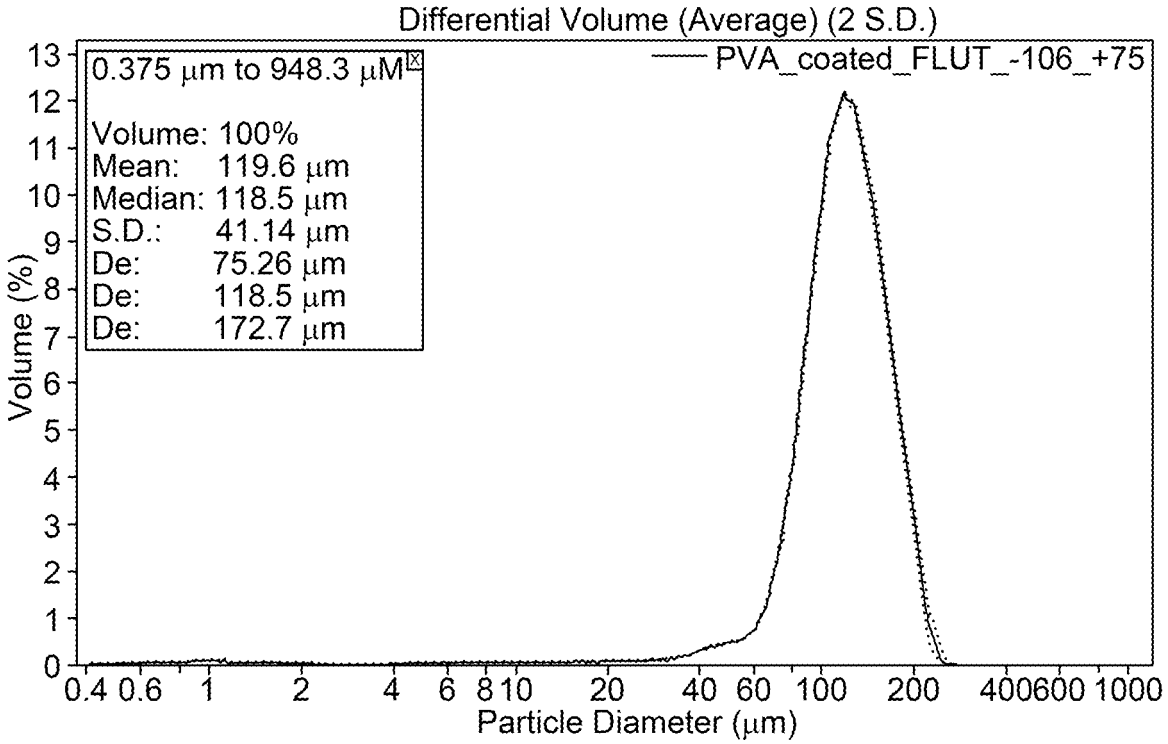

Differential Volume (Average) (2 S.D.)
PVA_coated_FLUT_-106_+75
0.375 µm to 948.3 µM
Volume: 100%
Mean: 119.6 µm
Median: 118.5 µm
S.D.: 41.14 µm
De: 75.26 µm
De: 118.5 µm
De: 172.7 µm
Volume (%)
Particle Diameter (µm)

FIG. 4A

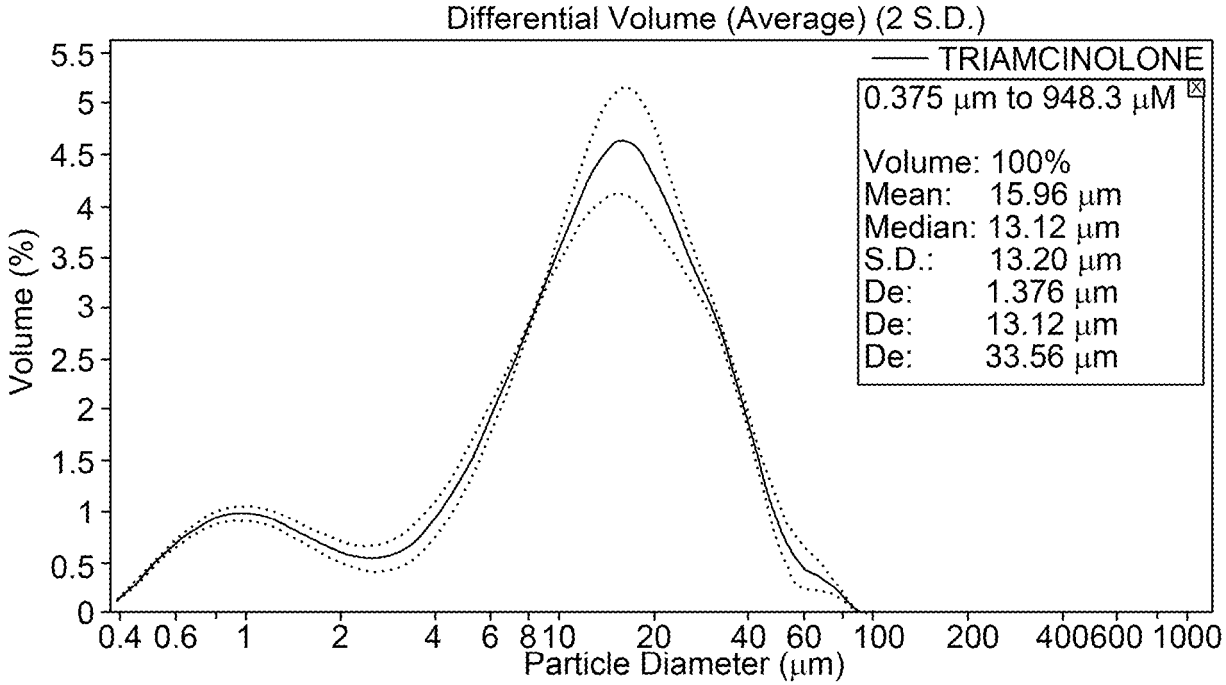

Differential Volume (Average) (2 S.D.)
TRIAMCINOLONE
0.375 µm to 948.3 µM
Volume: 100%
Mean: 15.96 µm
Median: 13.12 µm
S.D.: 13.20 µm
De: 1.376 µm
De: 13.12 µm
De: 33.56 µm
Volume (%)
Particle Diameter (µm)

FIG. 4B

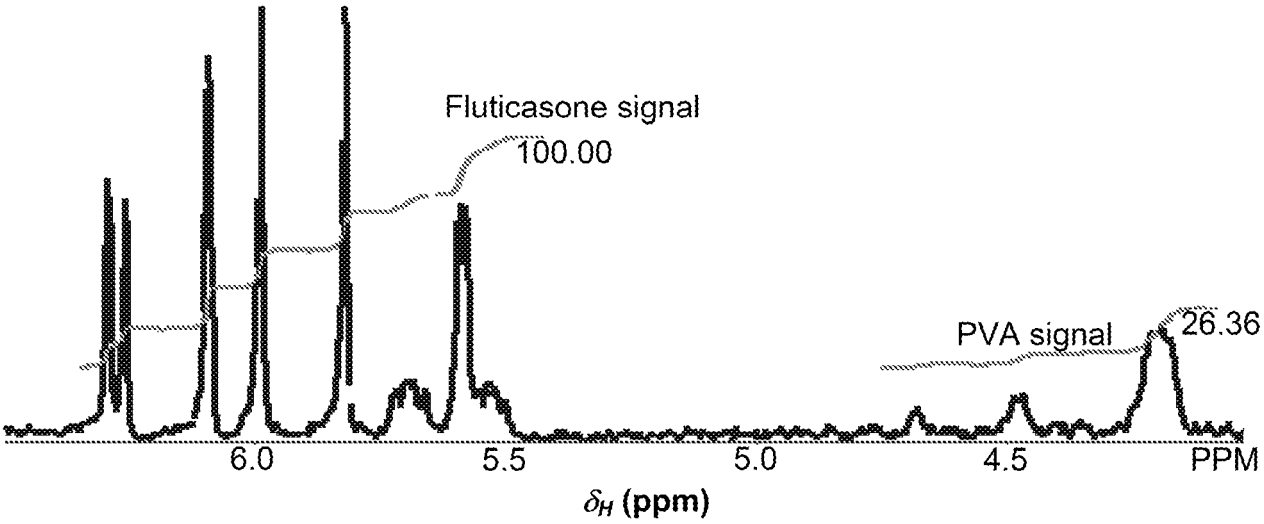

Fluticasone signal
100.00
PVA signal
26.36
6.0
5.5
5.0
4.5
PPM
δ_H (ppm)

FIG. 5

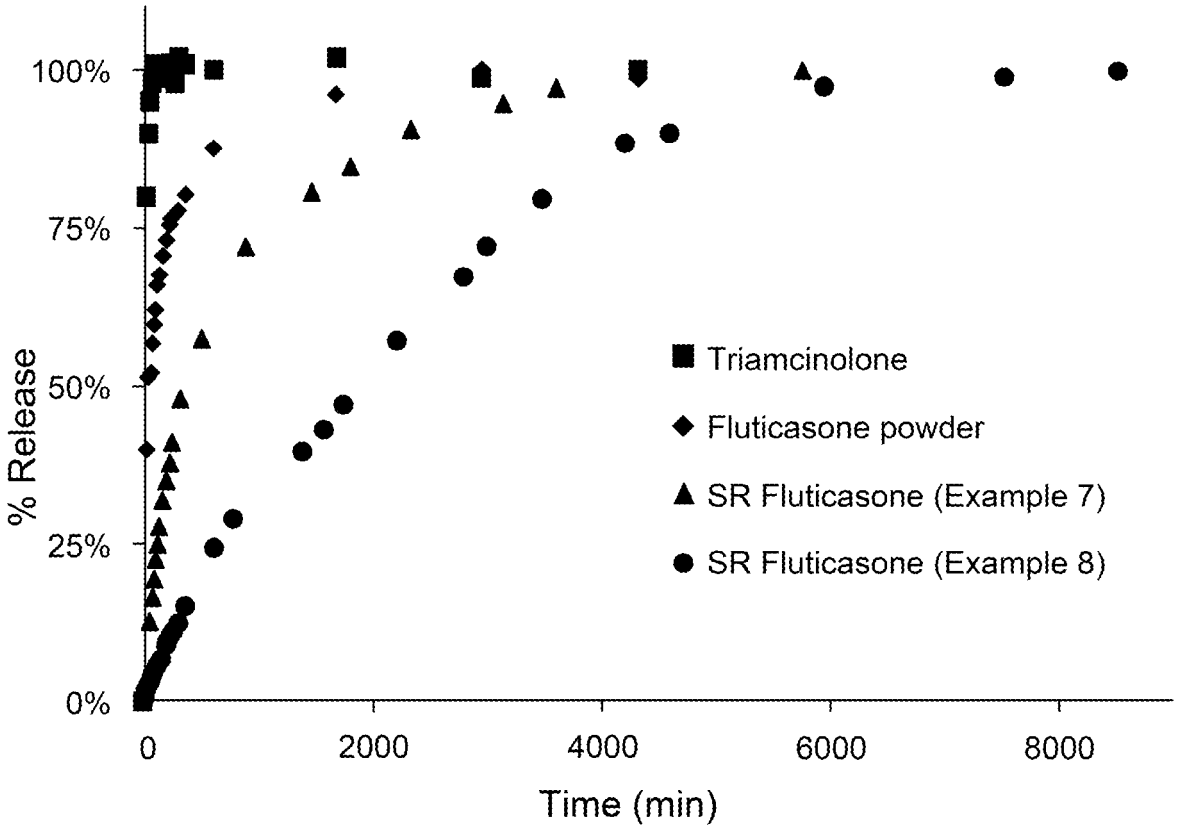

100%
75%
50%
25%
0%
% Release
0
2000
4000
6000
8000
Time (min)
Triamcinolone
Fluticasone powder
SR Fluticasone (Example 7)
SR Fluticasone (Example 8)

FIG. 6

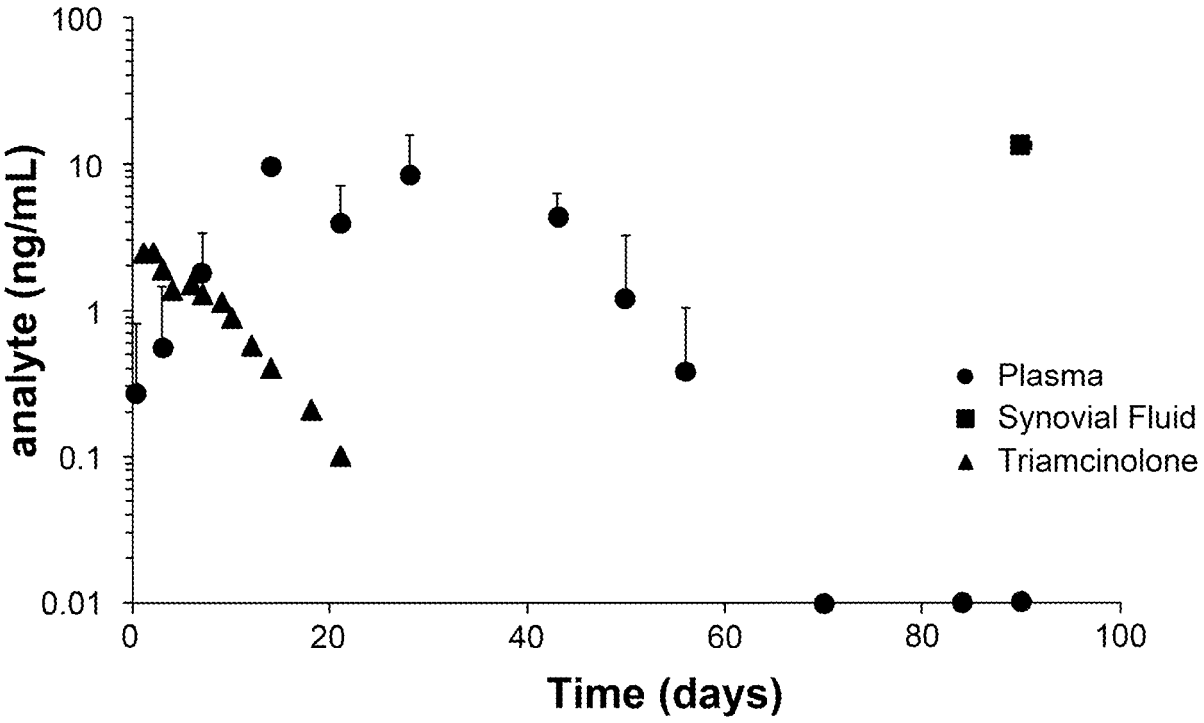

100
10
1
0.1
0.01
analyte (ng/mL)
0
20
40
60
80
100
Time (days)
Plasma
Synovial Fluid
Triamcinolone

FIG. 7

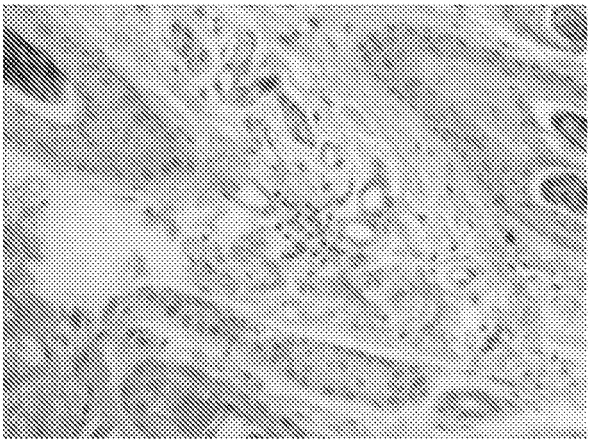


FIG. 8A

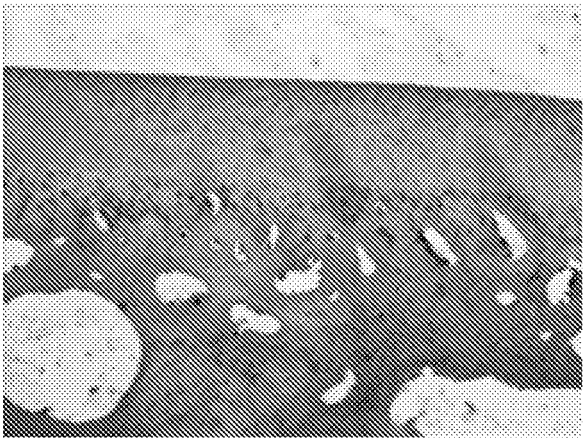


FIG. 8B

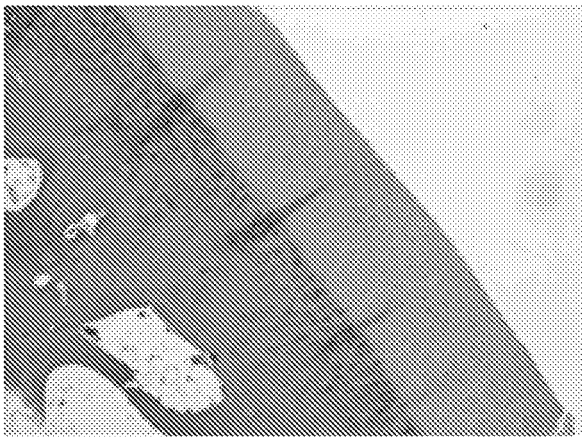


FIG. 8C

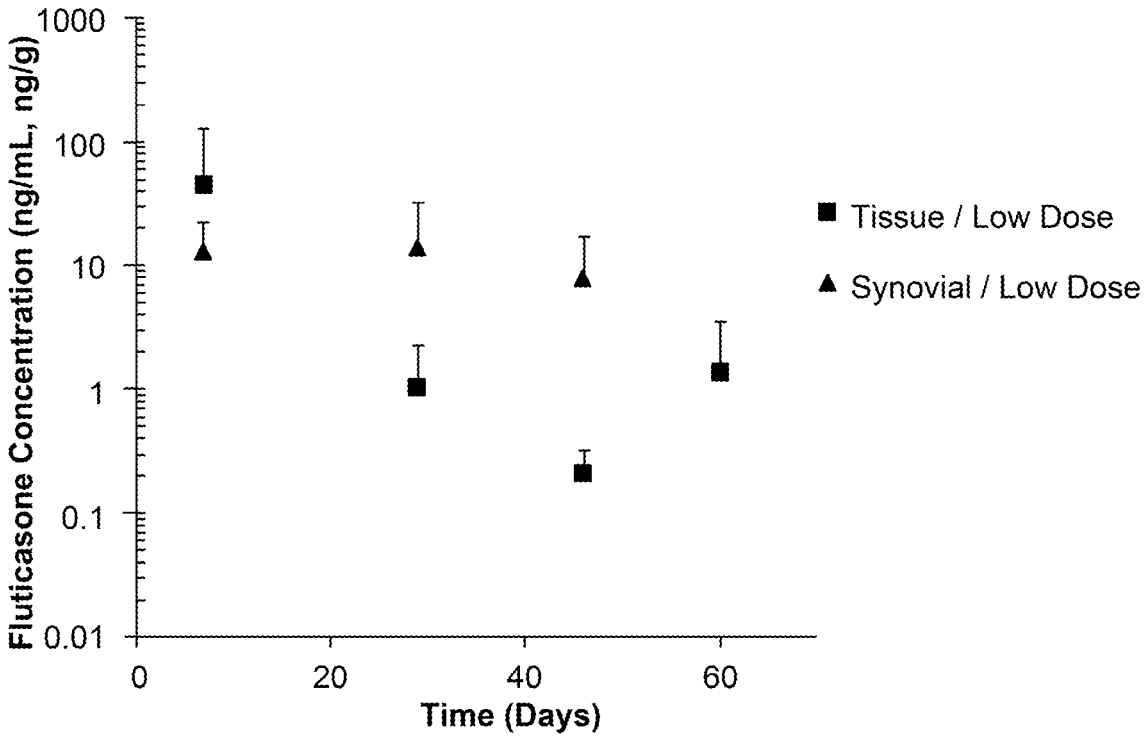

Fluticasone Concentration (ng/mL, ng/g)
1000
100
10
1
0.1
0.01
0
20
40
60
Time (Days)
Tissue / Low Dose
Synovial / Low Dose

FIG. 9

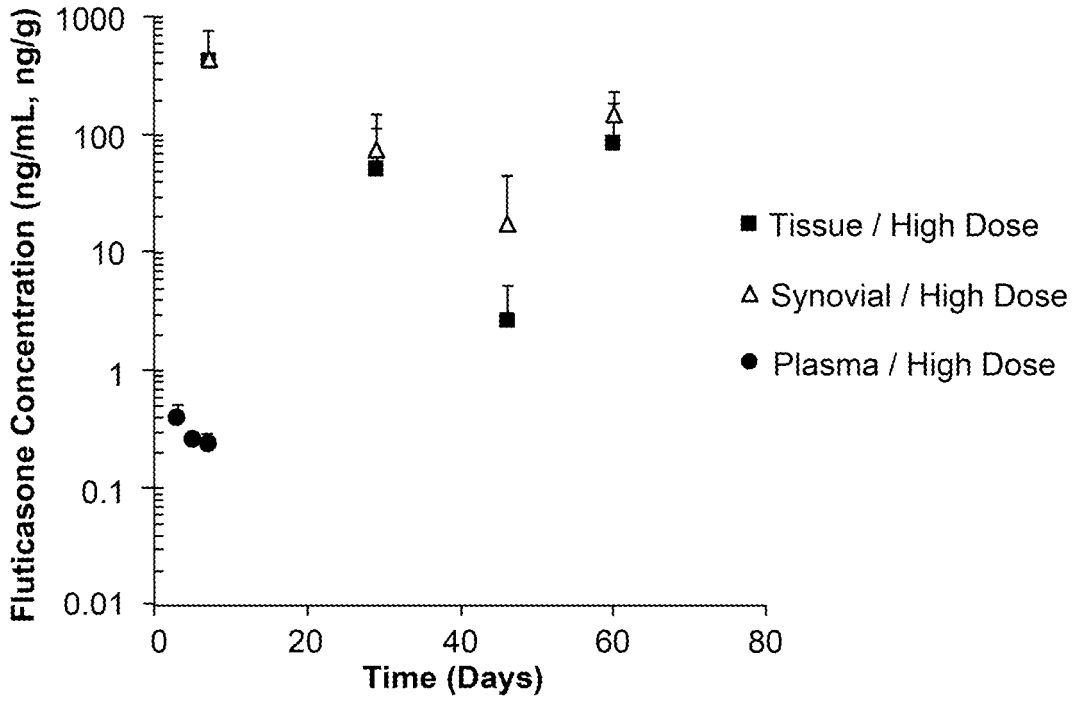

Fluticasone Concentration (ng/mL, ng/g)
1000
100
10
1
0.1
0.01
0
20
40
60
80
Time (Days)
Tissue / High Dose
Synovial / High Dose
Plasma / High Dose

FIG. 10

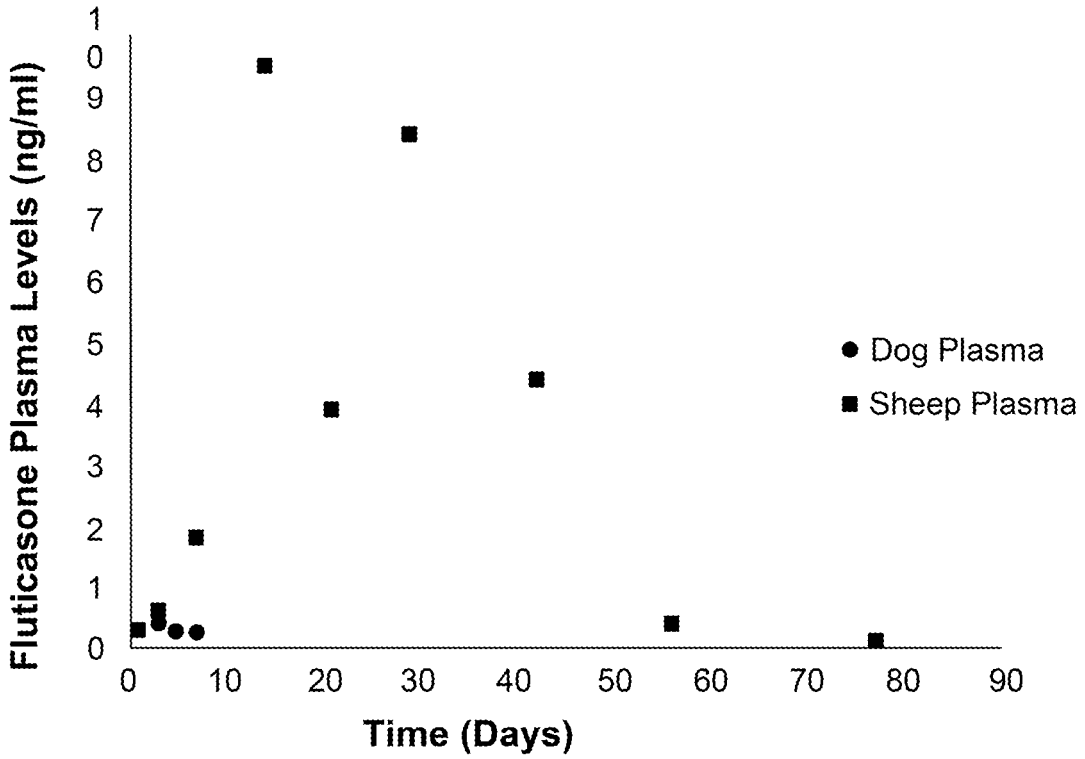

Fluticasone Plasma Levels (ng/ml)
1
0
9
8
7
6
5
4
3
2
1
0
0
10
20
30
40
50
60
70
80
90
Time (Days)
Dog Plasma
Sheep Plasma

FIG. 11

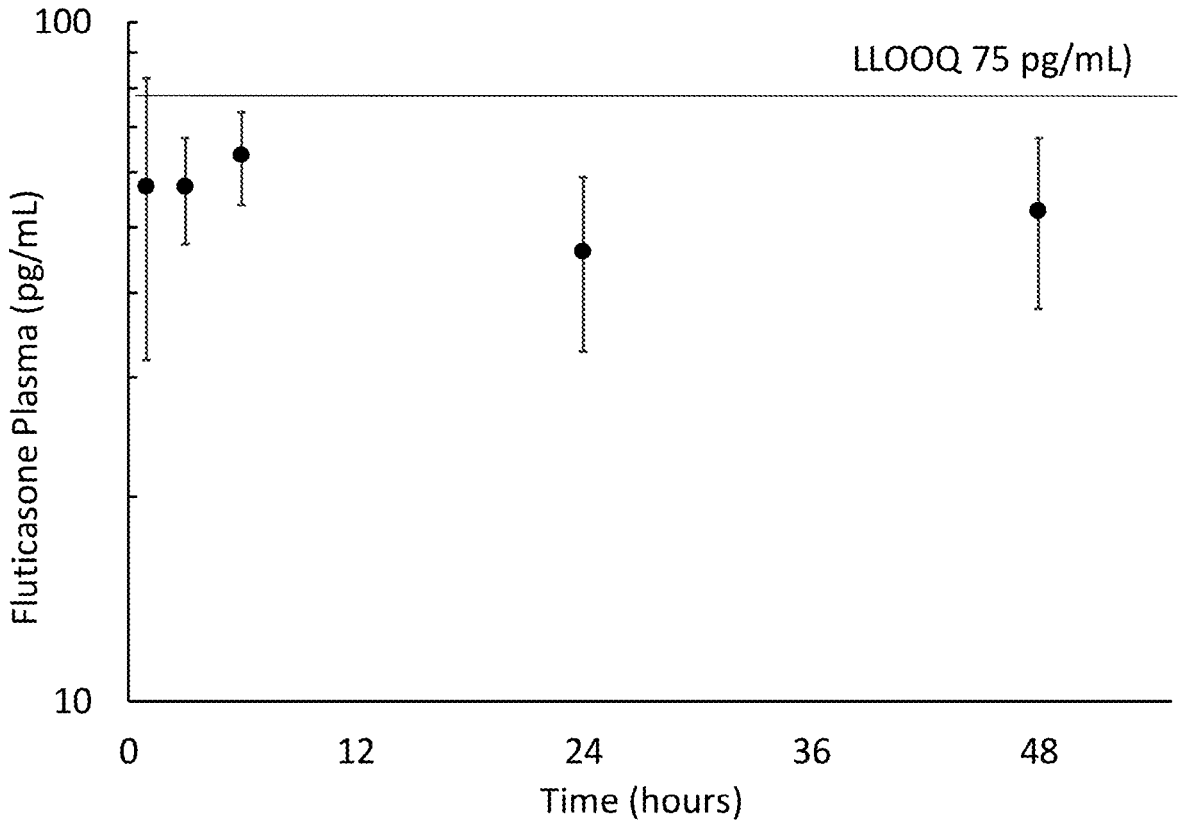

100
LLOOQ 75 pg/mL)
Fluticasone Plasma (pg/mL)
10
0
12
24
36
48
Time (hours)

FIG. 12

INTERNATIONAL SEARCH REPORT

WO 2014/153541

International application No
PCT/UPCT/US2014/031502

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K9/00 A61K9/50 A61K31/00
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, CHEM ABS Data, EMBASE, WPI Data, BIOSIS, FSTA

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2010/052896 A1 (JGC CORP [JP]; NAGAO TAKESHI [JP]; KAGAMI KAZUHIRO [JP]; OGAWA YASUAKI) 14 May 2010 (2010-05-14) example 1	1,7-26
A	WO 2010/007446 A1 (PROSONIX LTD [GB]; RUECROFT GRAHAM [GB]; PARIKH DIPESH [GB]; HIPKISS D) 21 January 2010 (2010-01-21) the whole document	1-55
A	US 2007/003619 A1 (SMITH THOMAS J [US]) 4 January 2007 (2007-01-04) the whole document	1-55
A	WO 2008/119033 A1 (EURAND INC [US]; VENKATESH GOPI M [US]) 2 October 2008 (2008-10-02) the whole document	1-55

☐ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
11 June 2014	20/06/2014

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Schüle, Stefanie

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INTERNATIONAL SEARCH REPORT

Information on patent family members

WO 2014/153541

International application No
PCT/UPCT/US2014/031502

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