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Dodd et al.

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(54) **FORMULATION OF DICLOFENAC**

(58) **Field of Classification Search**

(71) Applicant: **iCeutica Pty Ltd., Balcatta (AU)**

None

See application file for complete search history.

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(73) Assignee: **iCeutica Pty Ltd., Philadelphia, PA**
(US)

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(*) Notice: Subject to any disclaimer, the term of this
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U.S.C. 154(b) by 0 days.

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This patent is subject to a terminal dis-
claimer.

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(65) **Prior Publication Data**

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Related U.S. Application Data

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application No. PCT/AU2010/000471 on Apr. 23,
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(30) **Foreign Application Priority Data**

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(51) **Int. Cl.**

A61K 9/14 (2006.01)

A61K 31/196 (2006.01)

(Continued)

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CPC **A61K 9/4808** (2013.01); **Y10T 428/2982**
(2015.01); **A61K 9/143** (2013.01); **A61K 9/145**
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(57) **ABSTRACT**

The present invention relates to methods for producing par-
ticles of diclofenac using dry milling processes as well as
compositions comprising diclofenac, medicaments produced
using diclofenac in particulate form and/or compositions, and
to methods of treatment of an animal, including man, using a
therapeutically effective amount of diclofenac administered
by way of said medicaments.

24 Claims, 20 Drawing Sheets

Sample No.	Active material			Primary Matrix			Surfactant #1			Surfactant #2			Particle Size				Yield (%)	Variation		
	Name	Mass (g)	% w/w	Name	Mass (g)	% w/w	Name	Mass (g)	% w/w	Name	Mass (g)	% w/w	Time (mins.)	D(0.5) µm	% < 0.20 µm	% < 0.50 µm			% < 0.6 µm	% < 1.10 µm
T	DIC	4.95	99				SDS	0.05	1				30	117	0	0	0	1	4	
U	DIC	1.00	20	LAC	4.00	80							30	0.178	58	74	86	92	97	
V	DIC	2.00	20	MAN	8.00	80							30	0.2	50	69	84	91	97	
W	DIC	2.00	20	MAN	7.90	79	SDS	0.1	1				30	0.201	50	69	83	91	97	
X	DIC	2.00	20	MAN	7.90	79	SOS	0.1	1				30	0.195	51	71	85	92	97	
Y	NAA	1.75	35	LAC	3.2	65							20	2.9	18	23	25	26	38	
Z	NAA	1.75	35	LAC	3.25	64	P40S	0.05	1				20	0.373	33	45	56	70	87	
AA	NAA	1.75	35	LAC	3.25	64	SDS	0.05	1				20	0.293	38	50	60	66	75	
AB	NAA	4.0	40	LAC	5.9	59	P40S	0.1	1				120	0.285	37	52	66	75	82	
AC	NAA	4.0	40	LAC	6.0	60							120	6.1	0	0	0	0	8	
AD	NAA	1.40	35	MAN	2.60	65							20	0.171	58	73	82	86	88	
AE	NAA	1.40	35	MAN	2.52	63	SDS	0.08	2				20	0.131	76	90	96	96	98	
AF	NAA	1.2	30	MAN	2.8	70							20	0.208	48	64	75	79	84	
AG	NAA	1.2	30	MAN	2.76	69.0	SDS	0	1.0				20	0.173	58	75	86	91	96	
AH	NAA	1.2	30.0	LAC	2.8	70.0							20	0.396	33	44	53	58	70	
AI	NAA	1.2	30.0	TCG	2.8	70.0							20	3.1	18	24	27	27	37	
AJ	NAA	1.2	30.0	CAC	2.8	70.0							20	28	3	4	5	6	10	
AK	NAA	1	25.0	LAA	3	75.0							20	1.57	31	41	46	49	67	

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A61K 9/00 (2006.01)
- (52) **U.S. Cl.**
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9/0087 (2013.01); *A61K 9/14* (2013.01); *A61K*
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Sample No.	Active material			Primary Matrix			Surfactant #1			Surfactant #2			Time (mins.)	Particle Size					Yield (%)	Variations	
	Name	Mass (g)	% w/w	Name	Mass (g)	% w/w	Name	Mass (g)	% w/w	Name	Mass (g)	% w/w		D(0.5) µm	% < 0.20 µm	% < 0.30 µm	% > 0.5 µm	% > 1.0 µm			% > 2.0 µm
A	IND	1.20	12	LAC	8.80	88							30	0.223	45	61	71	77	89		
B	IND	1.20	12	LAC	8.70	87	SPS	0.1	1				30	0.215	47	64	84	83	93		
C	IND	1.20	12	LAC	8.70	87	SDS	0.1	1				30	0.189	53	73	88	95	99		
D	IND	1.20	12	LAC	8.70	87	SOS	0.1	1				30	0.203	49	69	84	92	97		
E	IND	1.20	12	LAC	8.70	87	B700	0.1	1				30	0.167	60	80	93	97	99		
F	IND	1.20	12	LAC	8.70	87	B76	0.1	1				30	0.192	52	72	89	96	99		
G	IND	1.20	12	LAC	8.70	87	SDC	0.1	1				30	0.191	52	67	77	83	93		
H	IND	1.20	12	LAC	8.70	87	SNS	0.1	1				30	0.225	44	63	79	88	96		
I	IND	1.20	12	LAC	8.70	87	LEC	0.1	1				30	0.230	44	61	75	85	95		
J	IND	0.5	10	LAC	4.50	90							20	0.237	44	57	65	73	85		
K	IND	0.5	10	LAC	4.45	89	P40S	0.05	1				20	0.169	58	72	80	89	97		
L	IND	0.5	10	LAC	4.45	89	DS	0.05	1				20	0.249	42	56	68	84	98		
M	IND	0.5	10	LAC	4.45	89	AS	0.05	1				20	0.190	52	67	76	84	92		
N	IND	1.0	20	LAC	3.95	79	SDS	0.05	1				30	0.435	24	38	53	67	83		
O	IND	1.0	20				SDS	4.00	80				30	2.612	0	0	0	6	34		
P	IND	4.95	99				SDS	0.05	1				30	1094	0	0	0	0	2		
Q	IND	1.0	20	LAC	4.00	80							30	5.128	0	0	0	0	8		
R	DIC	1.0	20	LAC	3.95	79	SDS	0.05	1				30	0.153	66	84	95	98	99		
S	DIC	1.0	20				SDS	4.00	80				30	3.173	0	0	0	3	24		

Figure 1A

Sample No.	Active material			Primary Matrix			Surfactant #1			Surfactant #2			Time (mins.)	Particle Size					Yield (%)	Variations
	Name	Mass (g)	% w/w	Name	Mass (g)	% w/w	Name	Mass (g)	% w/w	Name	Mass (g)	% w/w		D(0.5) µm	% > 0.20 µm	% > 0.30 µm	% > 0.5 µm	% > 1.0 µm		
T	DIC	4.95	99				SDS	0.051				30	117	0	0	0	1	4		
U	DIC	1.00	20	LAC	4.00	80						30	0.178	56	74	86	92	97		
V	DIC	2.00	20	MAN	8.00	80						30	0.2	50	69	84	91	97		
W	DIC	2.00	20	MAN	7.90	79	SDS	0.1	1			30	0.201	50	69	83	91	97		
X	DIC	2.00	20	MAN	7.90	79	SOS	0.1	1			30	0.195	51	71	85	92	97		
Y	NAA	1.75	35	LAC	3.2	65						20	2.9	18	23	25	26	38		
Z	NAA	1.75	35	LAC	3.25	64	P40S	0.051				20	0.373	33	45	56	70	87		
AA	NAA	1.75	35	LAC	3.25	64	SDS	0.051				20	0.293	38	50	60	65	75		
AB	NAA	4.0	40	LAC	5.9	59	P40S	0.1	1			120	0.285	37	52	66	75	82		
AC	NAA	4.0	40	LAC	6.0	60						120	6.1	0	0	0	0	8		
AD	NAA	1.40	35	MAN	2.60	65						20	0.171	58	73	82	86	88		
AE	NAA	1.40	35	MAN	2.52	63	SDS	0.082				20	0.131	76	90	95	96	98		
AF	NAA	1.2	30	MAN	2.8	70						20	0.208	48	64	75	79	84		
AG	NAA	1.2	30	MAN	2.76	69.0	SDS	0	1.0			20	0.173	58	75	86	91	96		
AH	NAA	1.2	30.0	LAC	2.8	70.0						20	0.396	33	44	53	58	70		
AI	NAA	1.2	30.0	TCD	2.8	70.0						20	3.1	18	24	27	27	37		
AJ	NAA	1.2	30.0	CAC	2.8	70.0						20	28	3	4	5	6	10		
AK	NAA	1	25.0	LAA	3	75.0						20	1.07	31	41	46	49	67		
AL	NAA	1	25.0	XYL	3	75.0						20	0.18	57	75	87	92	95		

Figure 1B

Sample No.	Active material			Primary Matrix			Surfactant #1			Surfactant #2			Time (mins.)	D(0.5) µm	Particle Size					Yield (%)	Variations
	Name	Mass (g)	% w/w	Name	Mass (g)	% w/w	Name	Mass (g)	% w/w	Name	Mass (g)	% w/w			% < 0.20 µm	% > 0.30 µm	% > 0.5 µm	% > 1.0 µm	% > 2.0 µm		
AM	NAA 1	25.0	75.0	MAA 3	75.0							20	0.153	66	85	96	98	99			
AN	NAA 1	25.0	75.0	TCD 3	75.0							20	0.331	35	48	57	62	72			
AO	HAL 1	10.0	90.0	LAC 9	90.0							40	2.123	0	0	0	0	5			
AP	HAL 1	10.0	89.0	LAC 8.9	89.0	LEC 0.1	1.0					40	0.135	74	90	97	98	99			
AQ	MET 1	10.0	90.0	LAC 9	90.0							40	4.727	0	0	0	0	4			
AR	MET 1	10.0	89.0	LAC 8.9	89.0	SDS 0.1	1.0					40	0.129	80	93	96	97	98			
AS	TRI 1	10.0	90.0	LAC 9	90.0							40	2.622	0	0	0	0	25			
AT	TRI 1	10.0	89.0	LAC 8.9	89.0	B700 0.1	1.0					40	0.128	82	96	98	98	99			
AU	SUL 1	10.0	90.0	LAC 9	90.0							40	0.388	27	42	56	69	86			
AV	SUL 1	10.0	89.0	LAC 8.9	89.0	SDS 0.1	1.0					40	0.455	6	26	55	78	96			
AW	MAN 1	10.0	90.0	LAC 9	90.0							40	0.198	50	71	88	97	97			
AX	MAN 1	10.0	89.0	LAC 8.9	89.0	B700 0.1	1.0					40	0.17	60	82	96	100	100			
AY	MAN 1	10.0	89.0	LAC 8.9	89.0	SDS 0.1	1.0					40	0.171	60	82	97	100	100			
AZ	MAN 1	10.0	89.0	LAC 8.9	89.0	LEC 0.1	1.0					40	0.181	56	78	95	100	100			
BA	MAN 2	20.0	79.0	LAC 7.9	79.0	SDS 0.1	1.0					40	0.212	47	68	86	96	98			
BB	MAN 3	30.0	69.0	LAC 6.9	69.0	SDS 0.1	1.0					40	0.258	36	58	81	94	97			
BC	MTX 1.5	30.0	69.0	LAC 3.5	69.0	P407 0.1	1.0					60	0.16	63	77	84	89	93		2	
BD	MTX 1.5	30.0	70.0	LAC 3.5	70.0							60	0.28	40	52	59	59	71		2	
BE	MTX 2.5	50.0	47.0	LAC 2.35	47.0	SDS 0.8	2.0	P407 0.1	2			60	0.148	67	83	92	98	99		2	

Figure 1C

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