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(54) **NATURAL COMBINATION HORMONE REPLACEMENT FORMULATIONS AND THERAPIES**

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(58) **Field of Classification Search**
None
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

1,967,351	A	7/1934	Dolay
2,232,438	A	2/1941	Butenandt
2,379,832	A	7/1945	Serini et al.
2,649,399	A	8/1953	Beall et al.
3,198,707	A	8/1965	Nomine et al.
3,478,070	A	11/1969	Stein et al.
3,526,648	A	9/1970	Bertin et al.
3,710,795	A	1/1973	Higuchi et al.
3,729,560	A	4/1973	Hagerman
3,729,566	A	4/1973	Ericsson et al.
3,755,573	A	8/1973	Berman
3,755,575	A	8/1973	Lerner
3,903,880	A	9/1975	Higuchi et al.
3,916,898	A	11/1975	Robinson
3,916,899	A	11/1975	Theeuwes et al.
3,921,636	A	11/1975	Zaffaroni
3,923,997	A	12/1975	Meuly
3,948,254	A	4/1976	Zaffaroni
3,971,367	A	7/1976	Zaffaroni
3,977,404	A	8/1976	Theeuwes
3,993,072	A	11/1976	Zaffaroni
4,008,719	A	2/1977	Theeuwes et al.
4,012,496	A	3/1977	Schopflin et al.
4,014,334	A	3/1977	Theeuwes et al.
4,014,987	A	3/1977	Heller et al.
4,016,251	A	4/1977	Higuchi et al.
4,071,623	A	1/1978	van der Vies
4,093,709	A	6/1978	Choi et al.
4,154,820	A	5/1979	Simoons
4,155,991	A	5/1979	Schopflin et al.
4,196,188	A	4/1980	Besins
4,215,691	A	8/1980	Wong
4,237,885	A	12/1980	Wong et al.
4,310,510	A	1/1982	Sherman et al.
4,327,725	A	5/1982	Cortese et al.
4,372,951	A	2/1983	Vorys
4,393,871	A	7/1983	Vorhauer et al.
4,402,695	A	9/1983	Wong
4,423,151	A	12/1983	Baranczuk
4,449,980	A	5/1984	Millar et al.
4,610,687	A	9/1986	Fogwell
4,629,449	A	12/1986	Wong
4,732,763	A	3/1988	Beck et al.
4,738,957	A	4/1988	Laurent et al.
4,756,907	A	7/1988	Beck et al.
4,762,717	A	8/1988	Crowley, Jr.
4,788,062	A	11/1988	Gale et al.
4,816,257	A	3/1989	Buster et al.
4,822,616	A	4/1989	Zimmermann et al.
4,865,848	A	9/1989	Cheng et al.

(Continued)

FOREIGN PATENT DOCUMENTS

CN	102258455		11/2011
EP	0275716	A1	7/1988
EP	0622075	A1	11/1994
EP	0785211	A1	1/1996
EP	0785212	A1	1/1996
EP	0811381	A1	6/1997
EP	2191833	A1	6/2010
GB	720561		12/1954
GB	848881	A1	9/1960
GB	874368		8/1961

(Continued)

OTHER PUBLICATIONS

Azeem et al., "Microemulsions as a Surrogate Carrier for Dermal Drug Delivery," Drug Development and Industrial Pharmacy, 35(5):525-547. 2009. Abstract Only.

(Continued)

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(57) **ABSTRACT**

Estrogen and progesterone replacement therapies are provided herein. Among others, the following formulations are provided herein: solubilized estradiol without progesterone; micronized progesterone without estradiol; micronized progesterone with partially solubilized progesterone; solubilized estradiol with micronized progesterone; solubilized estradiol with micronized progesterone in combination with partially solubilized progesterone; and solubilized estradiol with solubilized progesterone.

6 Claims, 4 Drawing Sheets