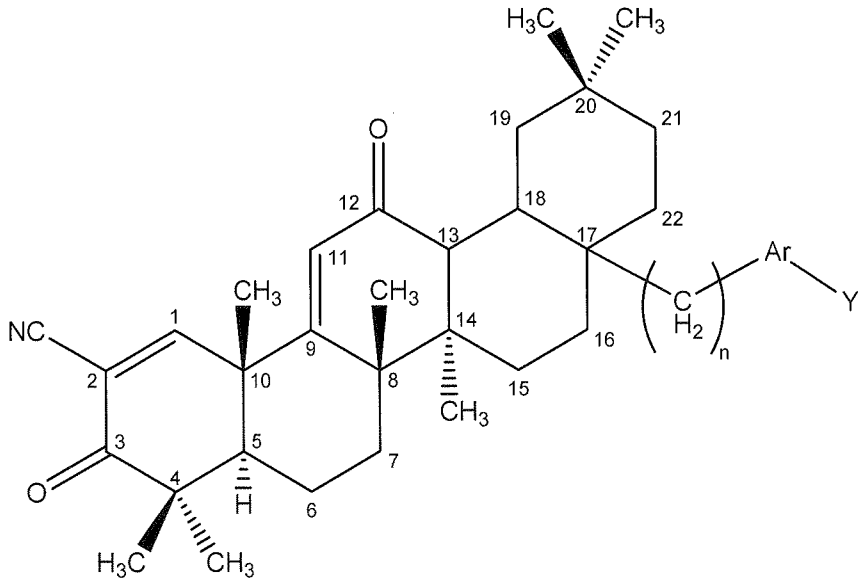
compounds have been less extensively characterized (Honda *et al.*, 2006). The pharmacology of these synthetic triterpenoid molecules is complex. Compounds derived from oleanolic acid have been shown to affect the function of multiple protein targets and thereby modulate the activity of several important cellular signaling pathways related to oxidative stress, cell cycle control, and inflammation (*e.g.*, Dinkova-Kostova *et al.*, 2005; Ahmad *et al.*, 2006; Ahmad *et al.*, 2008; Liby *et al.*, 2007a). Derivatives of betulinic acid, though they have shown comparable anti-inflammatory properties, also appear to have significant differences in their pharmacology compared to OA-derived compounds (Liby *et al.*, 2007b). Given that the biological activity profiles of known triterpenoid derivatives vary, and in view of the wide variety of diseases that may be treated or prevented with compounds having potent antioxidant and anti-inflammatory effects, and the high degree of unmet medical need represented within this variety of diseases, it is desirable to synthesize new compounds with diverse structures that may have improved biological activity profiles for the treatment of one or more indications.

SUMMARY ~~OF THE INVENTION~~

The present disclosure ~~provides~~ describes novel synthetic triterpenoid derivatives with anti-inflammatory and/or antioxidant properties, pharmaceutical compositions, and methods for their manufacture, and methods for their use.

In one aspect, there are provided compounds of the formula:



(I),

wherein:

n is 0-3;

Ar is heteroarenediyl$_{(C\leq 8)}$ or a substituted version thereof; and

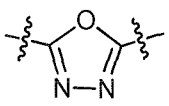
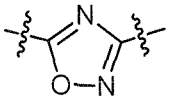
Y is:

hydrogen, hydroxy, halo, amino, or cyano or –NCO; or

alkyl$_{(C\leq 8)}$, alkenyl$_{(C\leq 8)}$, alkynyl$_{(C\leq 8)}$, aryl$_{(C\leq 12)}$, aralkyl$_{(C\leq 12)}$, heteroaryl$_{(C\leq 8)}$, heterocycloalkyl$_{(C\leq 12)}$, acyl$_{(C\leq 12)}$, alkoxy$_{(C\leq 8)}$, aryloxy$_{(C\leq 12)}$, acyloxy$_{(C\leq 8)}$, alkylamino$_{(C\leq 8)}$, dialkylamino$_{(C\leq 8)}$, arylamino$_{(C\leq 8)}$, aralkylamino$_{(C\leq 8)}$, alkylthio$_{(C\leq 8)}$, acylthio$_{(C\leq 8)}$, alkylsulfonylamino$_{(C\leq 8)}$, or substituted versions of any of these groups;

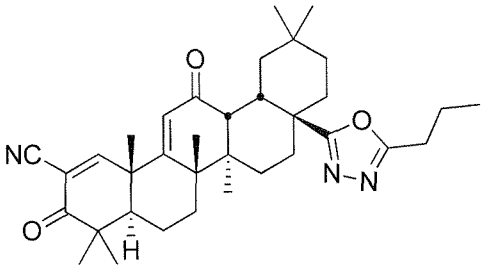
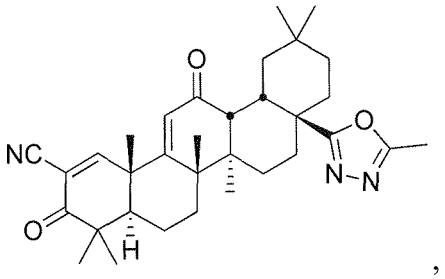
or a pharmaceutically acceptable salt thereof.

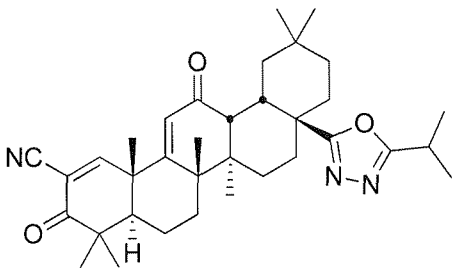
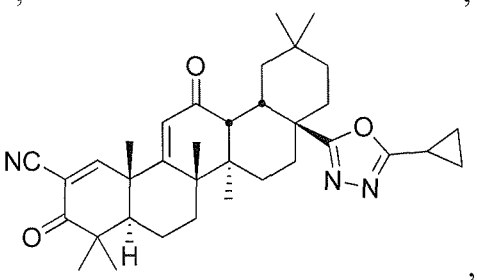
In some ~~embodiments~~examples, Y is –H. In some examples~~embodiments~~, Y is alkyl$_{(C\leq 4)}$, for example, methyl, *n*-propyl, isopropyl or cyclopropyl. In some examples~~embodiments~~, Y is substituted alkyl$_{(C\leq 4)}$, for example, methoxymethyl.

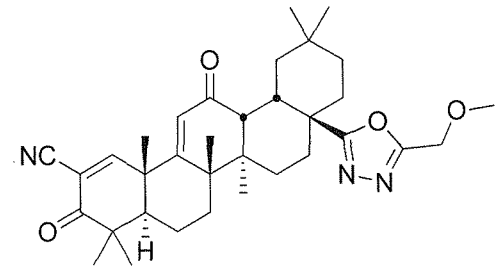
In some ~~embodiments~~examples, Ar is  or .

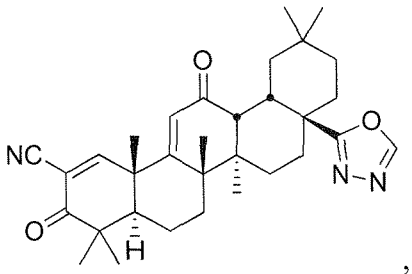
In some examples~~embodiments~~, n = 0. In other examples~~embodiments~~, n = 1.

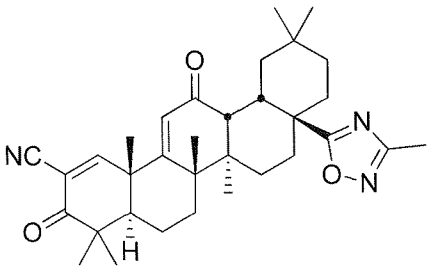
In some examples~~embodiments~~, the compound is selected from the group consisting of:

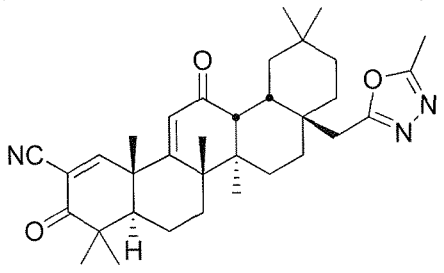
, ,

, ,



,


,


, and


or a pharmaceutically acceptable salt of any of the above formulas.

In some examplesaspects, there are provided pharmaceutical compositions comprising one or more of the above compounds and an excipient. In other examplesaspects there are provided methods of treating and/or preventing a disease or a disorder in patients in need thereof, comprising administering to such patients one or more of the above compounds in an amount sufficient to treat and/or prevent the disease or disorder. In one aspect, the present invention refers to use of a compound as defined herein in the manufacture of a medicament for treating and/or preventing a disease or a disorder in a patient in need thereof.

Other objects, features and advantages of the present disclosure will become apparent from the following detailed description. It should be understood, however, that the detailed description and the specific examples, while indicating specific embodiments of the invention, are given by way of illustration only, since various changes and modifications within the spirit and scope of the invention will become apparent to those skilled in the art from this detailed description. Note that simply because a particular compound is ascribed to one particular generic formula doesn't mean that it cannot also belong to another generic formula.

11. A pharmaceutical composition comprising:

a) the compound according to any one of claims 1-10; and

b) an excipient.

12. Use of a compound according to any one of claims 1-10 in the manufacture of a medicament for~~A method of~~ treating and/or preventing a disease or a disorder in a patient in need thereof~~, comprising administering to the patient a compound according to any one of claims 1-10 in an amount sufficient to treat and/or prevent the disease or disorder~~.