essential for viral replication and gene expression. The functional polypeptides are released from the polyproteins by extensive proteolytic processing which is one of the crucial steps in the life cycle of coronaviruses. The virus will not be packaged without the proteolysis. This is primarily achieved by the 33.1-kDa main protease (MPro), which is also known as 3C-like protease (3CLPro).

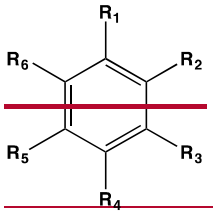
Members of the coronavirus's family include virus strains having different phylogenetic origin (thelancet.com; doi.org/10.1016/S0140-6736 (20)30251-8) and causing different severity in mortality and morbidity. As such, treatment for coronavirus infection varies depending on the specific strains that causes the infection. So far, there is no approved antiviral drug treatment for any coronavirus. Because of the conservation of the critical residues and its functional importance, we consider 3CLPro can be an important target for the design of ubivquitous anti-coronaviral drugs for the infection.

SUMMARY

The present disclosure is based on the unexpected observation that exemplary compounds having the structure of Formula (I) described herein successfully inhibited the protease activity of 3CLPro of SARS-CoV-2 and inhibited SARS-CoV-2 replication in cells. Further, it was observed that compounds of Formula (I) with high numbers of galloyl moieties showed better inhibitory activity against 3CLPro of SARS-CoV-2 that those having lower numbers of galloyl moieties. Moreover, exemplary Formula (I) compounds (*e.g.*, SNB01) showed presence in pulmonary tissues upon oral administration in an animal model. All the discoveries reported herein show that compounds of Formula (I) would be expected to be effective in inhibiting coronavirus such as SARS-CoV-2 and thus alleviating conditions caused by coronavirus infection.

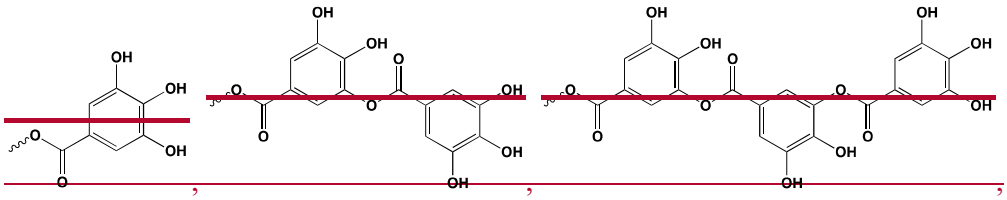
In one aspect, the present disclosure features a use of a composition in the manufacture of a medicament for treating coronavirus infection, wherein the composition comprises a compound of a formula selected from the group consisting of:

(a) ~~Formula (Ic)~~

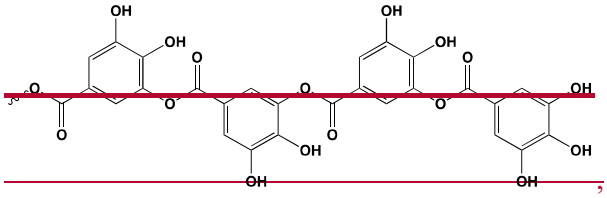


(Ic),

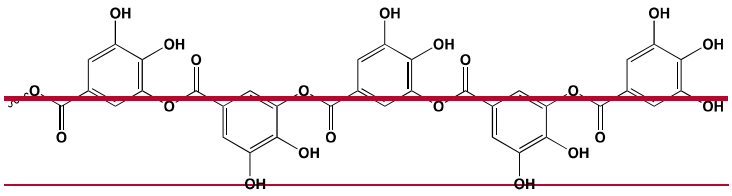
in which R_1, R_2, R_3, R_4, R_5, and R_6 are each, independently, selected from the group consisting of:



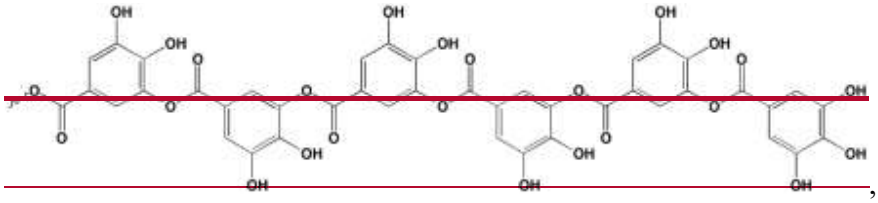
,



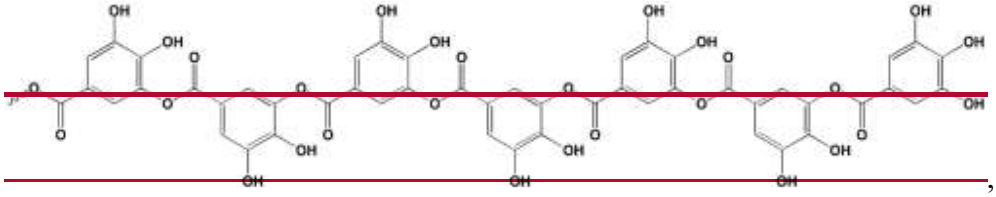
,



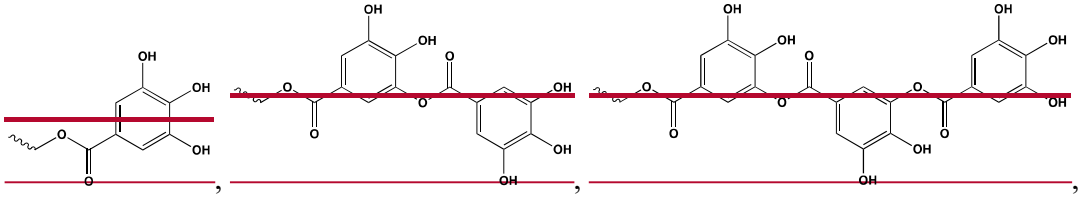
,



,



,

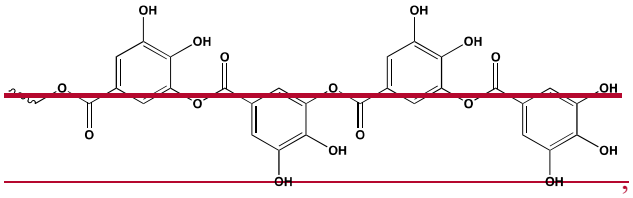


,

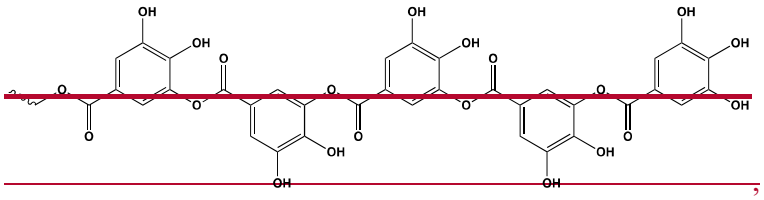
,

,

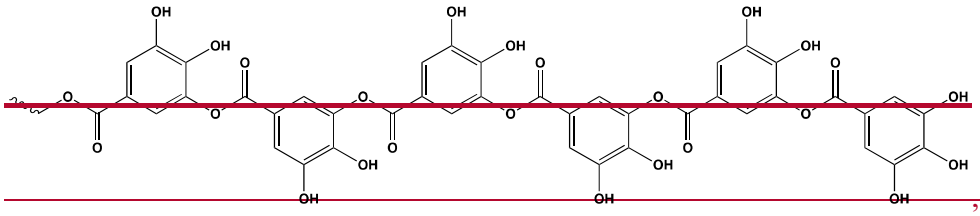
,



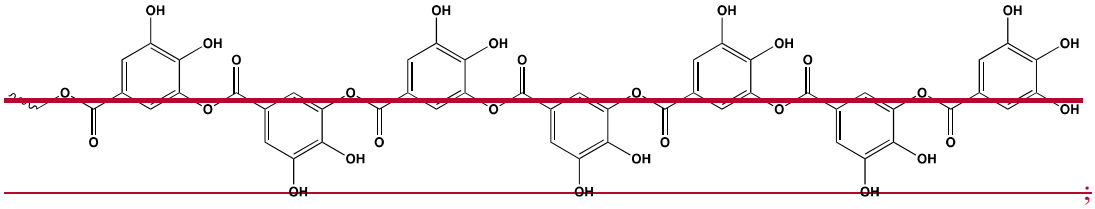
,



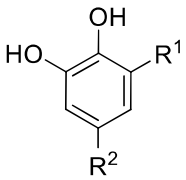
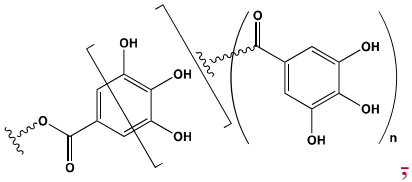
,

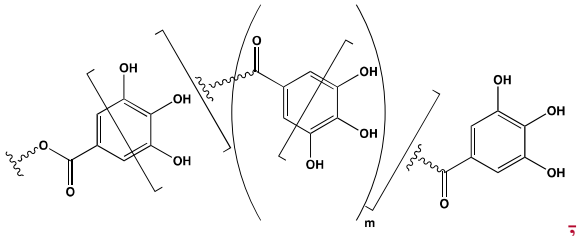
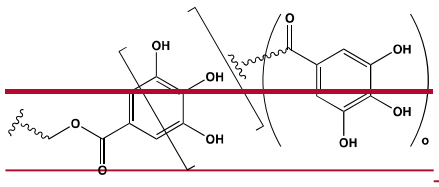


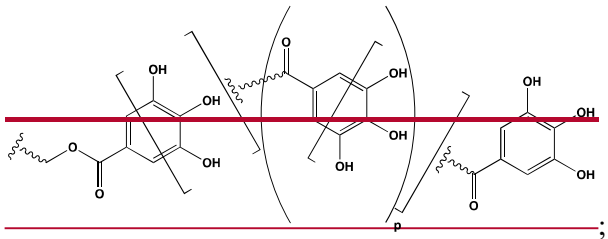
, and

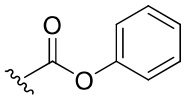


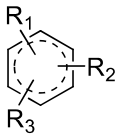
;

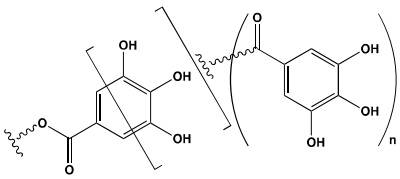
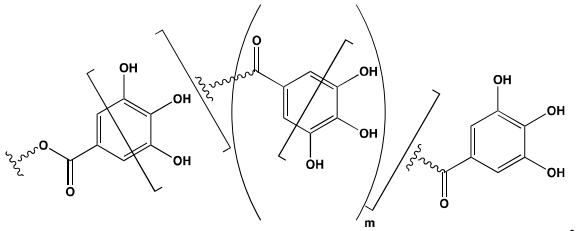
~~(b)~~ Formula (Id)  (Id), in which R^1 is  ~~,~~ and

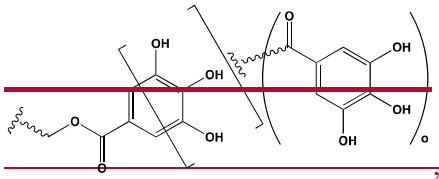
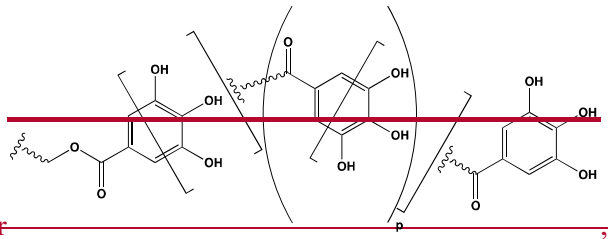
 ~~,~~  ~~, or~~

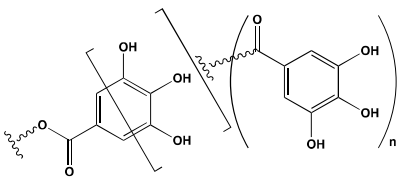
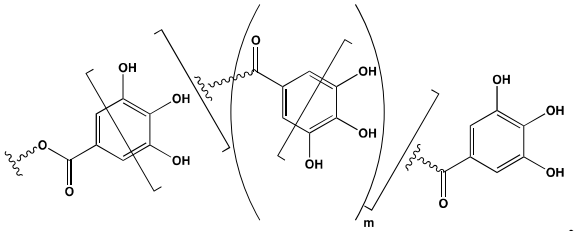


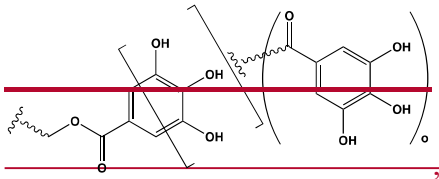
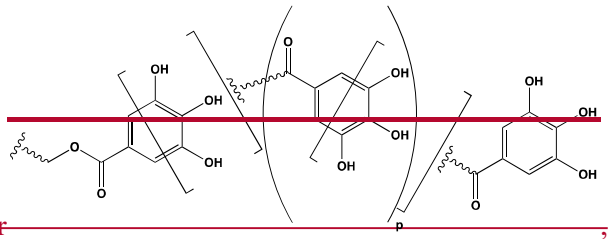
; and R^2 is –COOH or  , wherein n is 1;

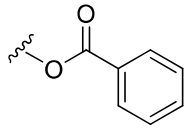
(~~e~~b) Formula (Ie)  (Ie), in which at least one of R^1, R^2, and R^3 is

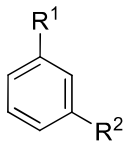
 ~~,~~or  ,

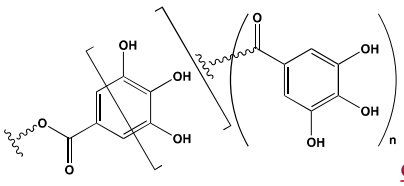
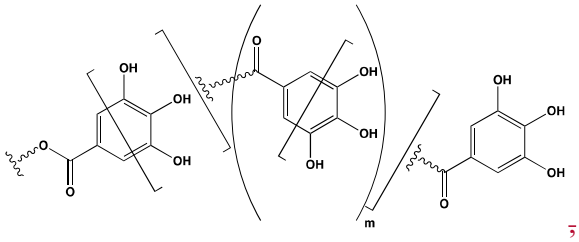
 ~~, or~~  ~~,~~ and the remaining of R^1, R^2, and R^3 each independently are ~~selected from the group consisting of~~

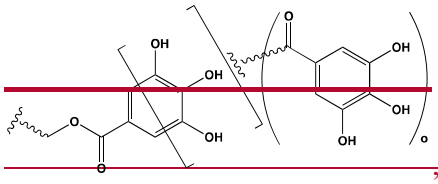
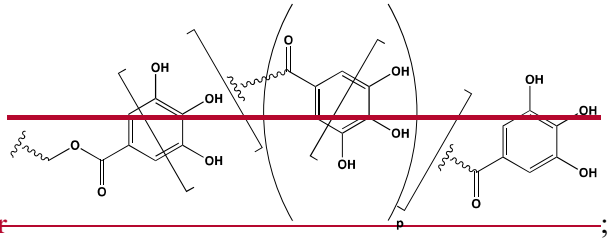
 ,  ,

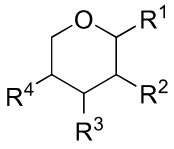
 ~~, or~~  ~~, and~~or

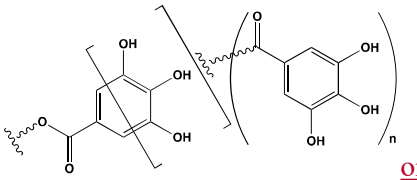
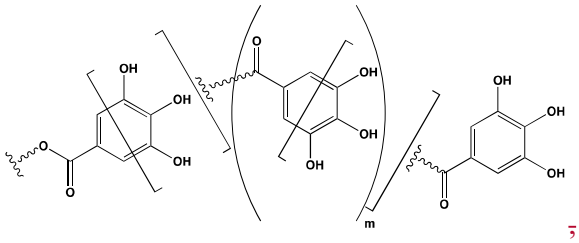
 ;

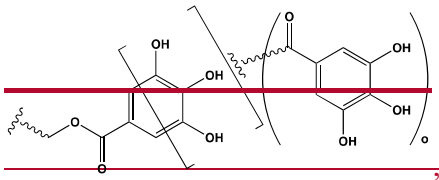
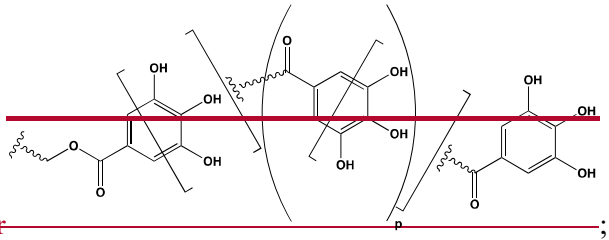
(~~d~~c) Formula (If):  (If), in which each of R^1 and R^2, independently, is

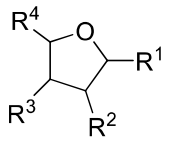
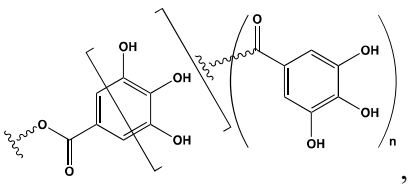
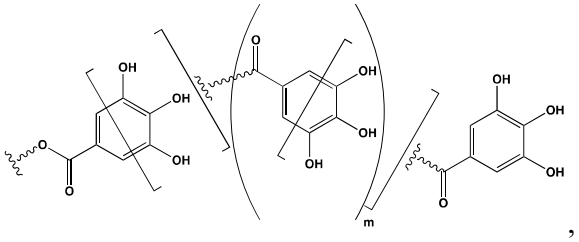
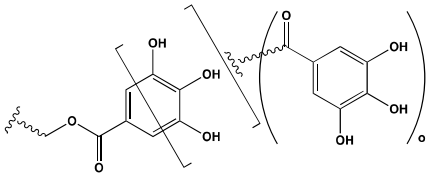
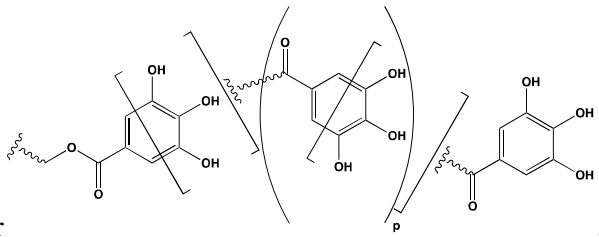
 or,  ,

 , or  ;

(~~e~~d) Formula (Ig):  (Ig), in which each of R^1, R^2, R^3, and R^4, independently, is

 or,  ,

 , or  ; and

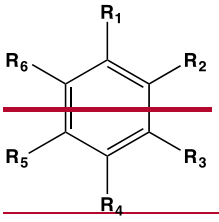
(f~~e~~) Formula (Ih):  (Ih), in which each of R^1, R^2, R^3, and R^4, independently, is  ,  ,  , or  , wherein n and o are independently 0 or 1 and wherein ~~n~~ p and m are independently 1, 2, 3, 4 or 5.

Accordingly, one example of the present disclosure features a method of inhibiting coronavirus and/or treating coronavirus infection, the method comprising administering to a subject in need thereof an effective amount of a composition, wherein the composition comprises one or more compounds of Formula (I):

What Is Claimed Is:

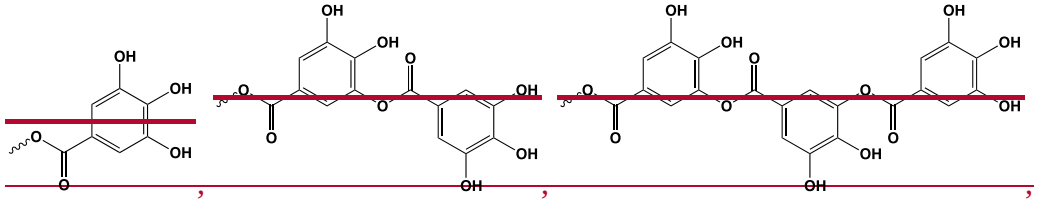
1. Use of a composition in the manufacture of a medicament for treating coronavirus infection, wherein the composition comprises a compound of a formula selected from the group consisting of:

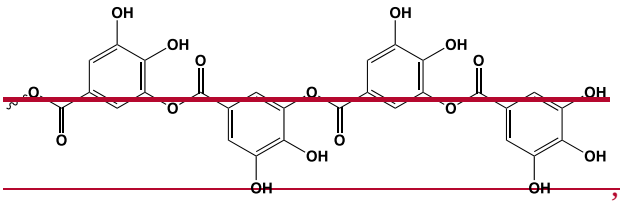
(a) ~~Formula (Ic)~~

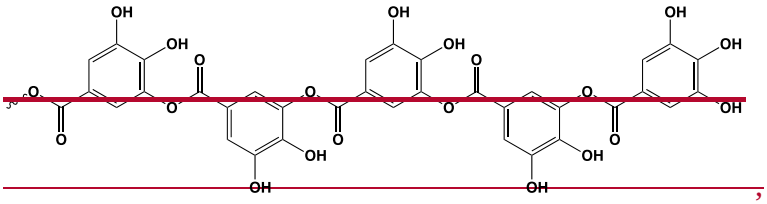


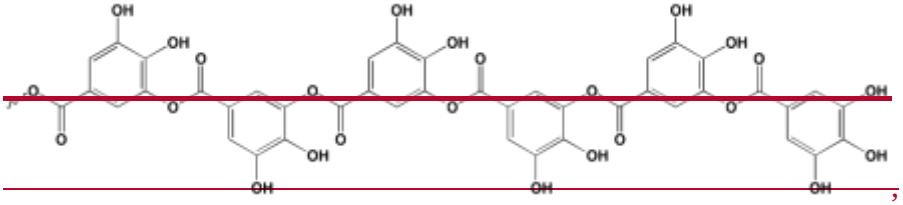
~~(Ic),~~

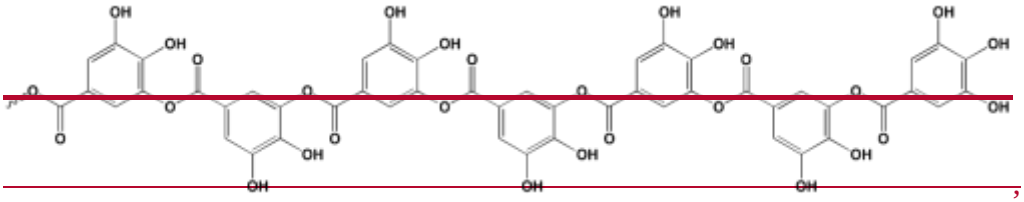
~~in which R_1, R_2, R_3, R_4, R_5, and R_6 are each, independently, selected from the group consisting of:~~



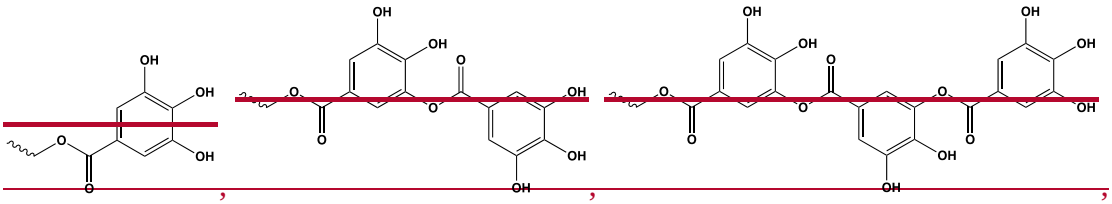




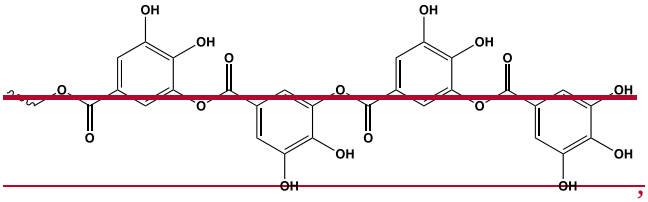




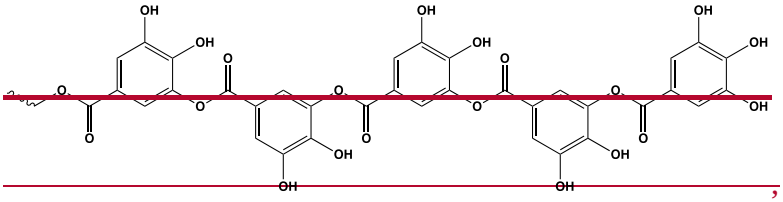
,



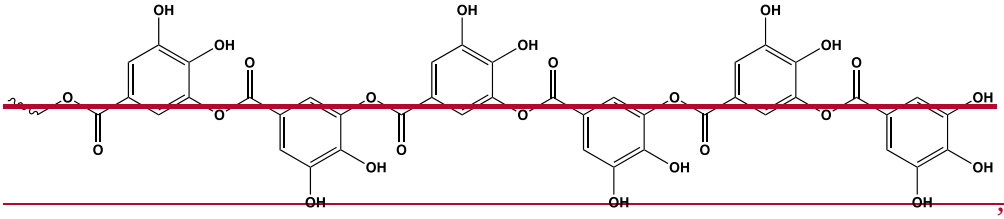
, , ,



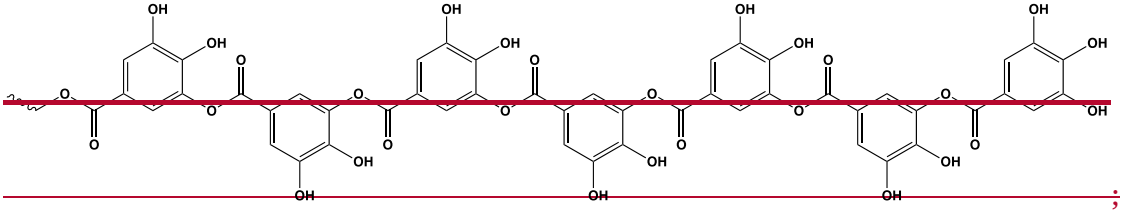
,



,

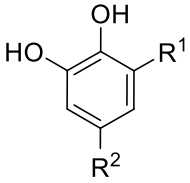


, ~~and~~

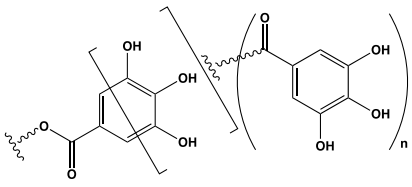


;

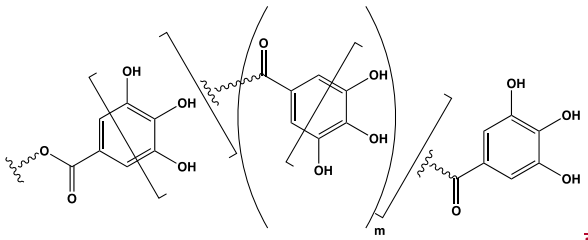
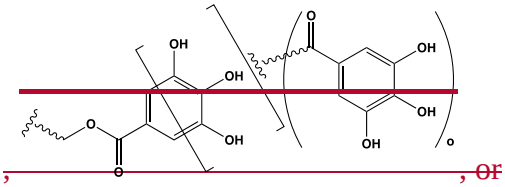
~~(b)~~ Formula (Id)

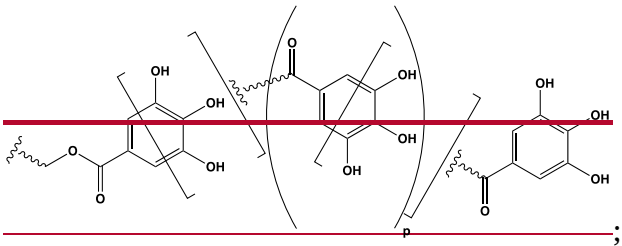
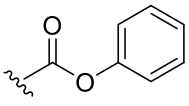


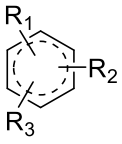
(Id), in which R^1 is

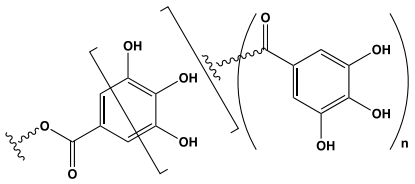
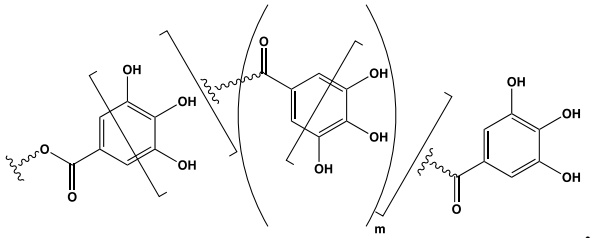


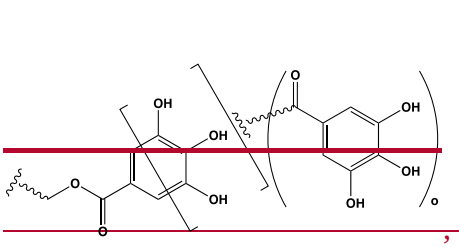
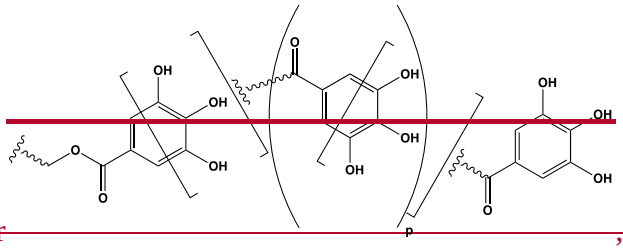
and ~~,~~

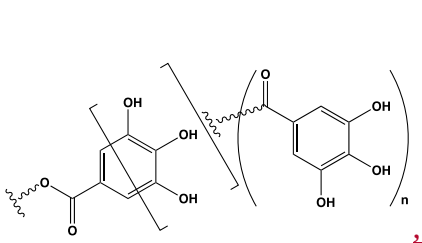
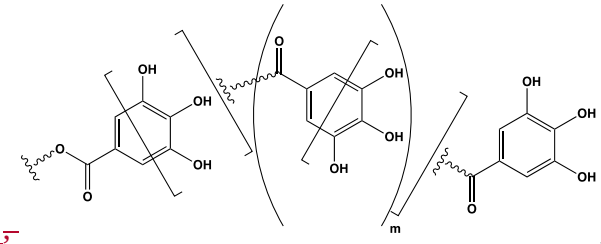


, ~~or~~

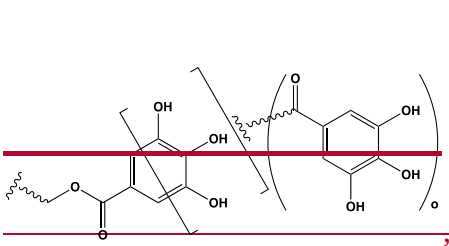

; and R^2 is –COOH or  , wherein n is 1;

(b~~c~~) Formula (Ie)  (Ie), in which at least one of R^1, R^2, and R^3 is

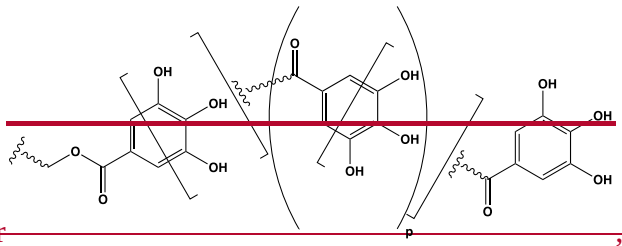

or~~,~~ 
,


, or 
, and the remaining of R^1, R^2, and R^3 each independently are ~~selected from the group consisting of~~

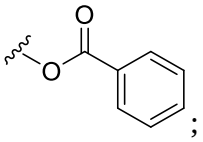

~~,~~ 
,



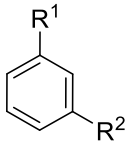
, or

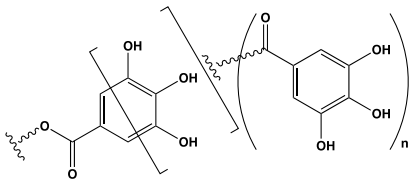


, or and

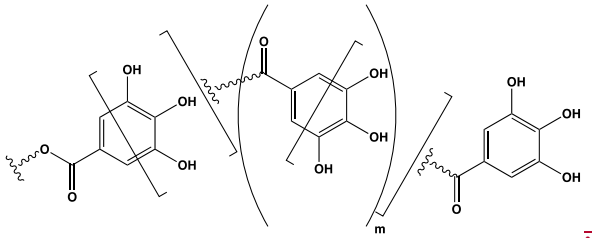


;

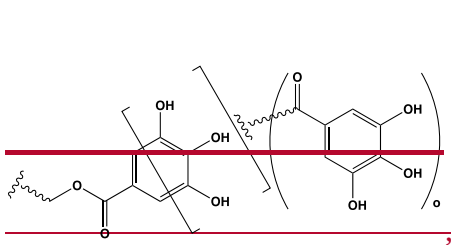
(cd) Formula (If):  (If), in which each of R^1 and R^2, independently, is

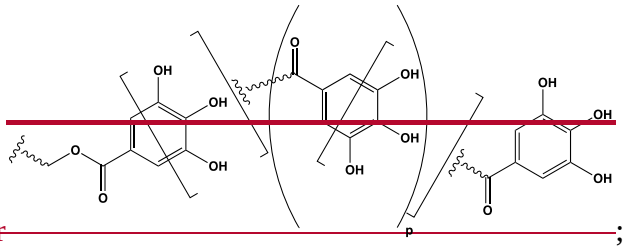


or,

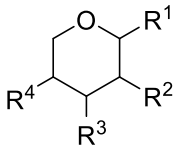


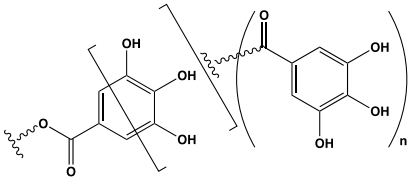
;



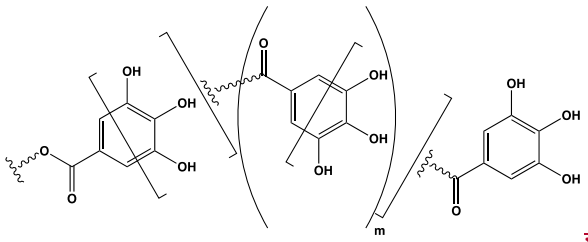


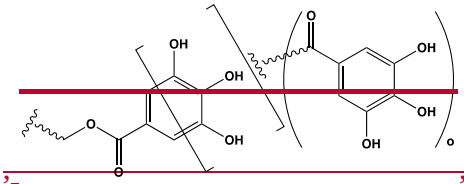
, or ;

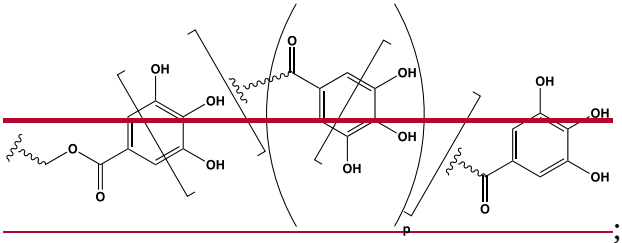
(de) Formula (Ig):  (Ig), in which each of R^1, R^2, R^3, and R^4, independently, is

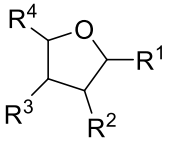


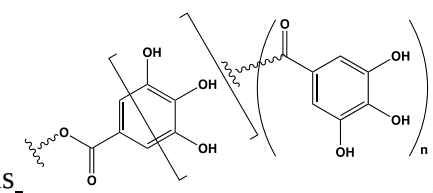
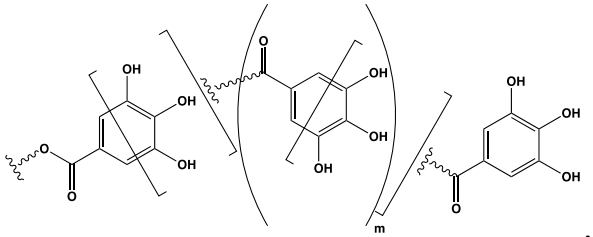
or,

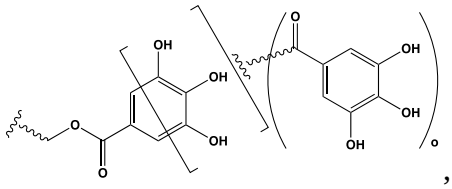
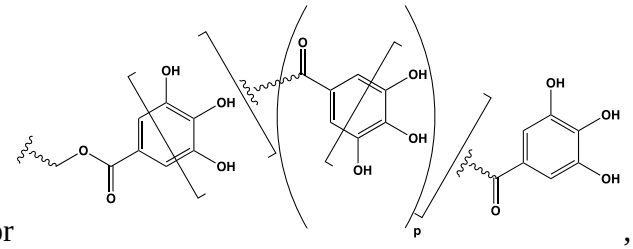


,  , or

 ; and

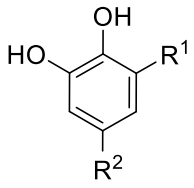
(e~~f~~) Formula (Ih):  (Ih), in which each of R^1, R^2, R^3, and R^4, independently,

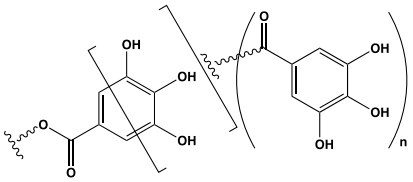
is  ,  ,

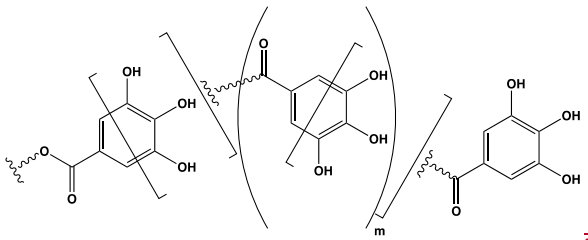
 , or  ,

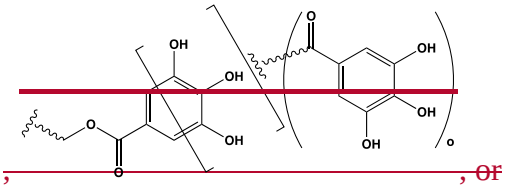
wherein n and o are independently 0 or 1 and wherein p~~n~~ and m are independently 1, 2, 3, 4 or 5.

2. The use of claim 1, wherein the compound is of the Formula (Id):

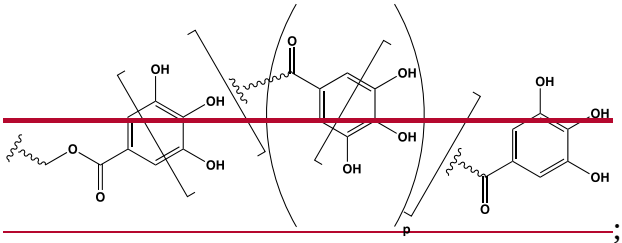


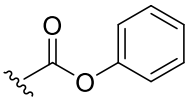
(Id), in which R^1 is  or~~and,~~





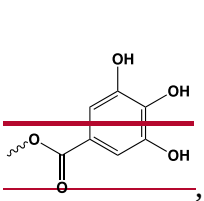
~~, or~~

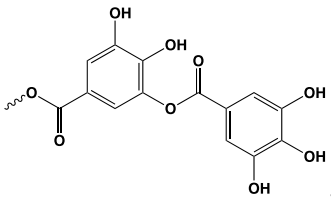


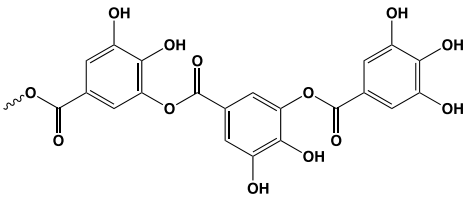
; and R^2 is –COOH or  , wherein n is 1.

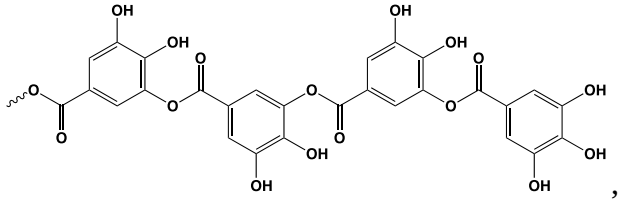
5

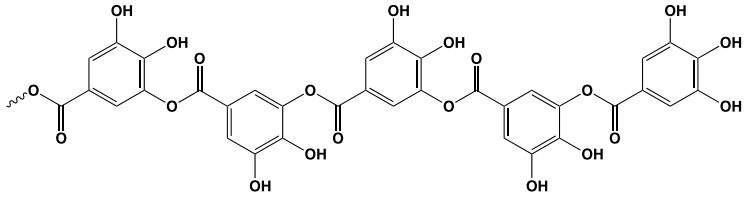
3. The use of claim 2, wherein R^1 is selected from the group consisting of:

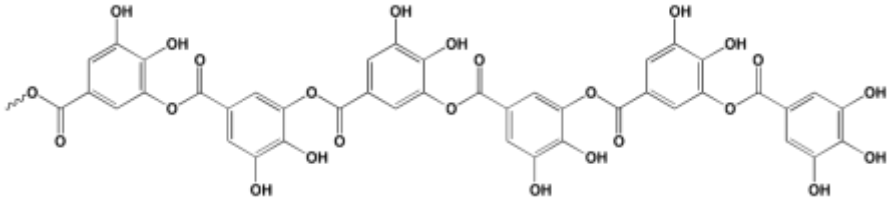
 ,

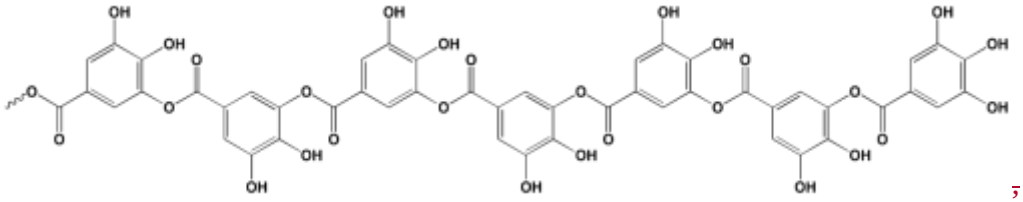
 ,

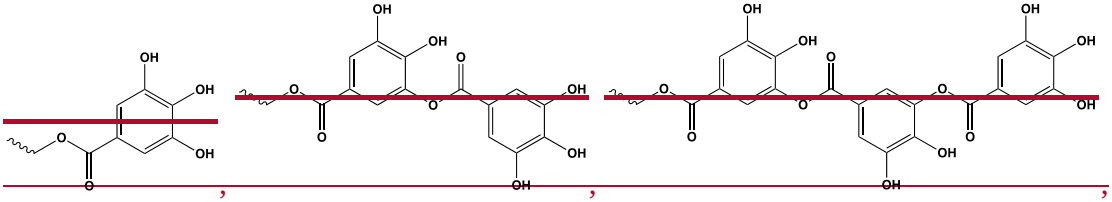
 ,

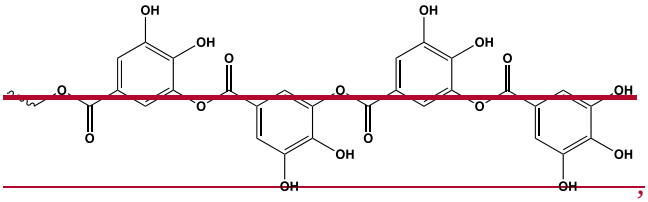
 ,

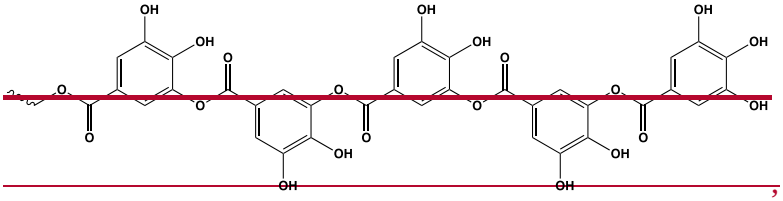
 ,

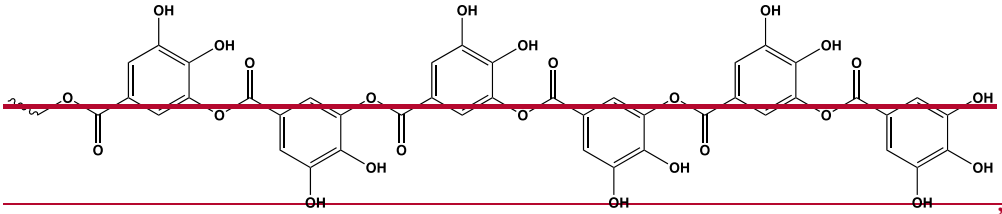

, and

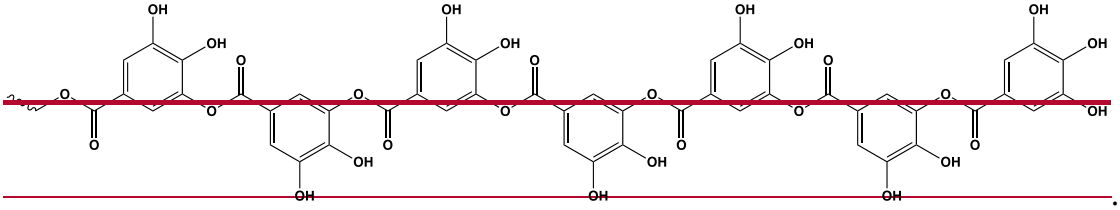

;


,

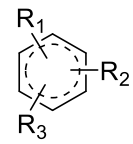

,

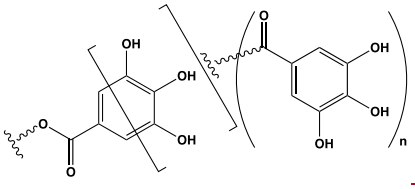

,

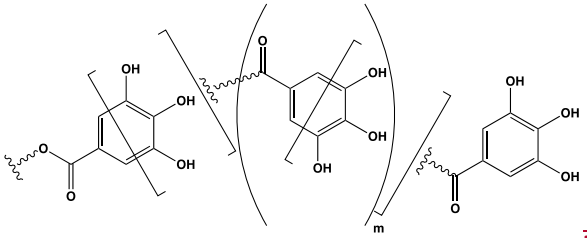

, and

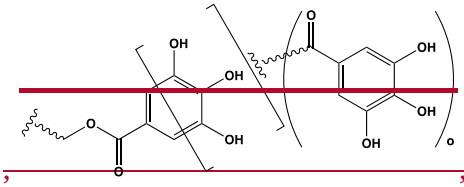

.

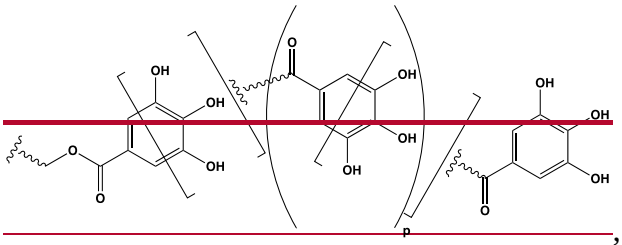
4. The use of claim 3, wherein the compound of Formula (Id) is phenol 3G, phenol 5G, phenol 7G, ~~Compound 14, Compound 18,~~ or Compound 149.

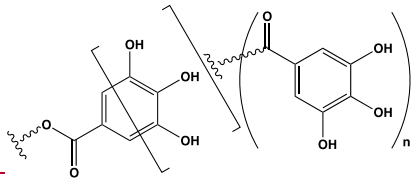
5. The use of claim 1, wherein the compound is of the Formula (Ie) 

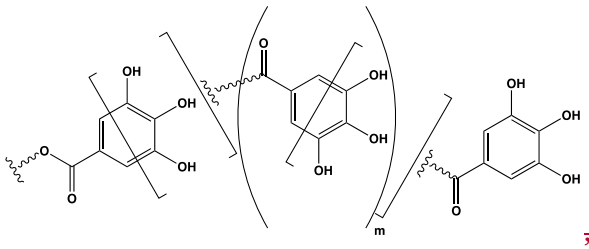
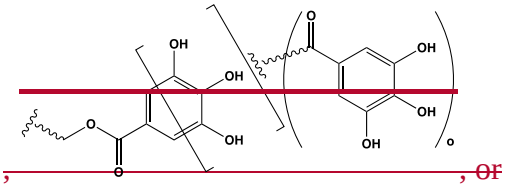
(Ie), in which at least one of R^1, R^2, and R^3 is  or~~,~~

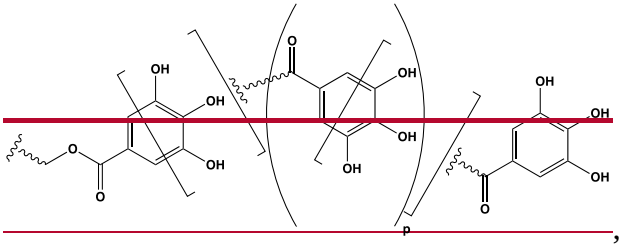
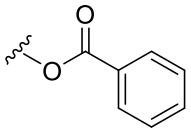


~~,~~  ~~, or~~

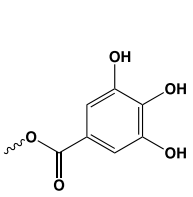
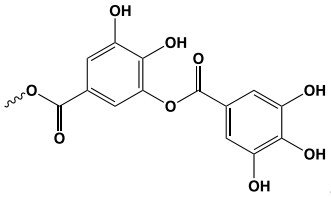
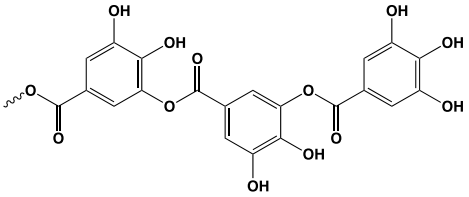
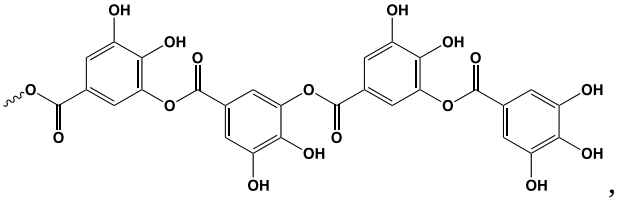
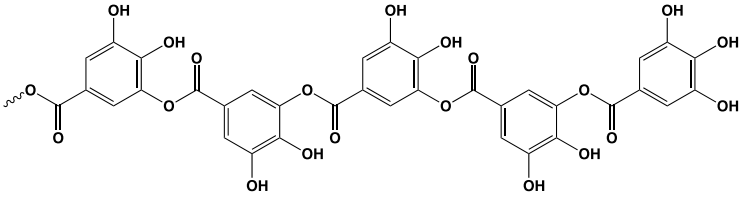
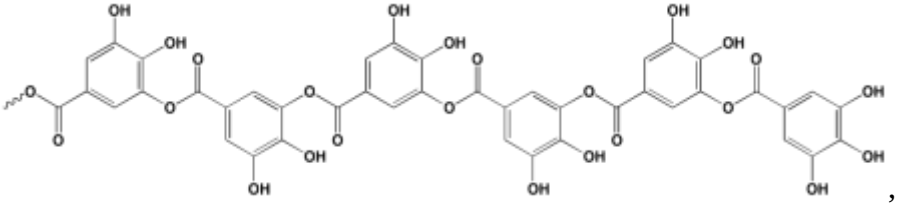


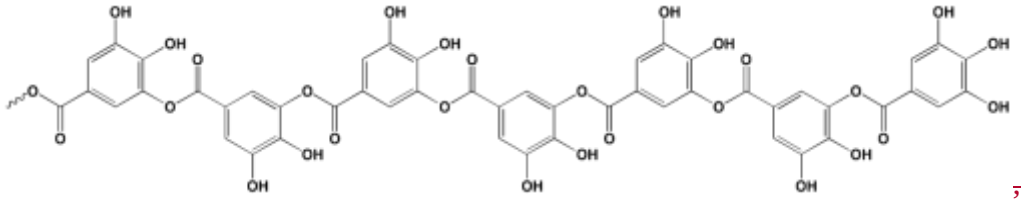
, and the remaining of R^1, R^2, and R^3 each independently are ~~selected from the group consisting of~~  or~~,~~

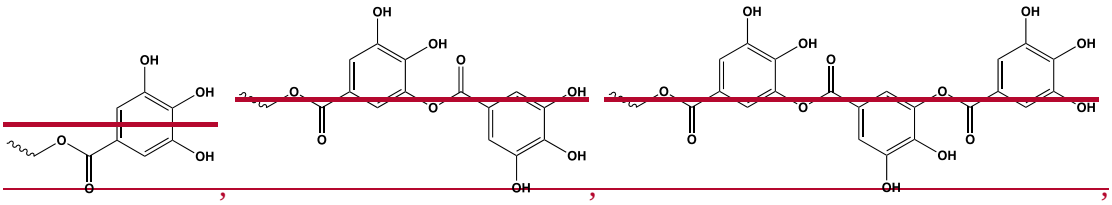


, ~~or~~

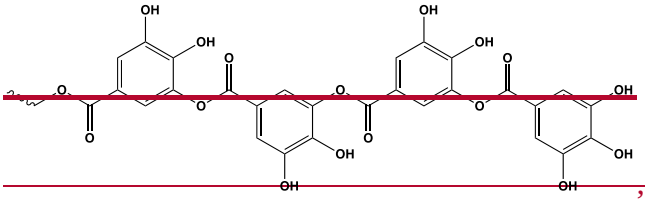

, and 
.

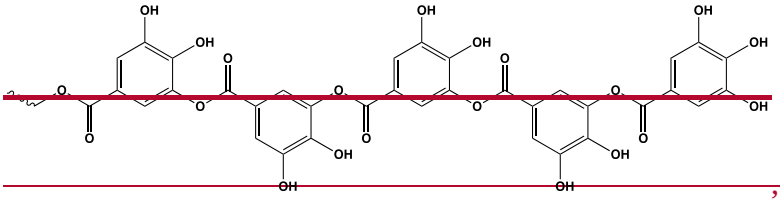
6. The use of claim 5, wherein each of R^1, R^2, and R^3, independently, is selected from the group consisting of:

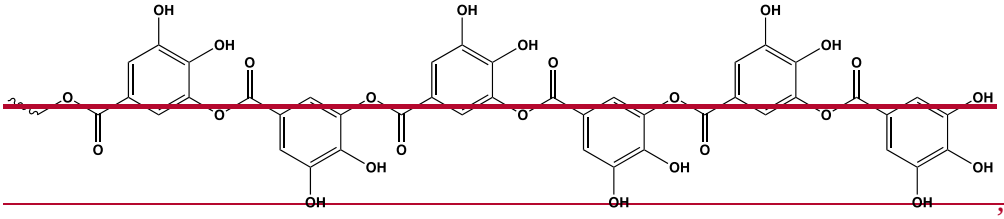

,

,

,

,

,

, and

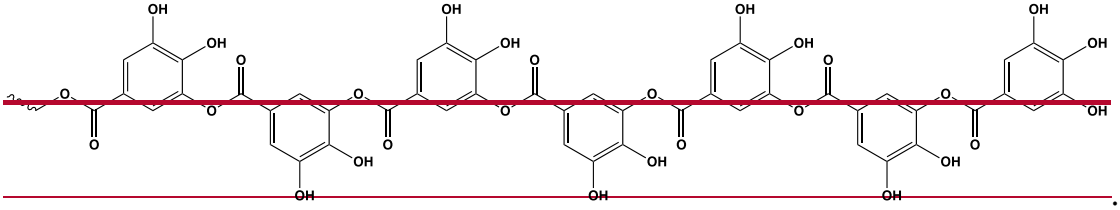

;


,

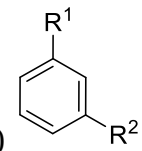
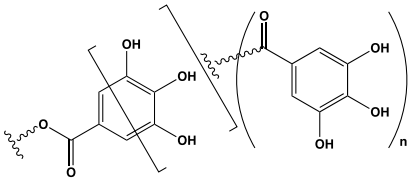

,

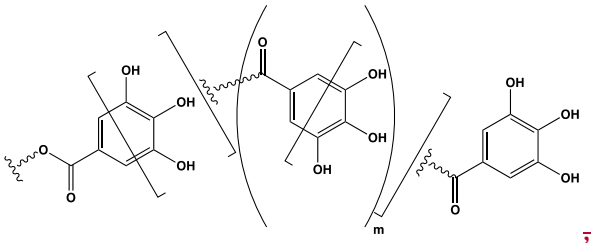

,


, and

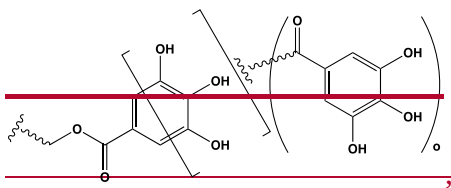

.

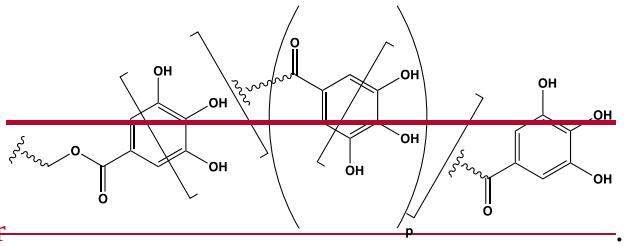
7. The use of claim 5, wherein the compound of Formula (Ie) is ~~phloroglucinol 6G,~~ phloroglucinol 9G, ~~phloroglucinol 12G,~~ phloroglucinol 15G, phloroglucinol 21G, or Compound 103.

8. The use of claim 1, wherein the compound is of the Formula (If)  (If), in which each of R^1 and R^2, independently, is  or,

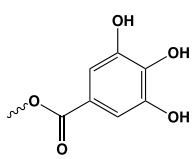
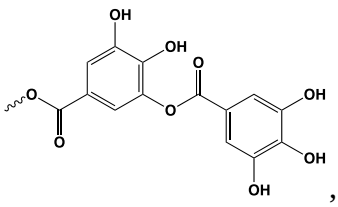
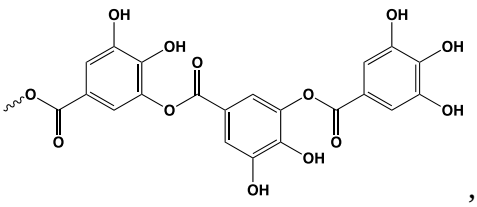


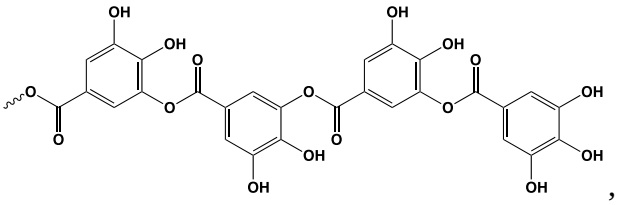
,

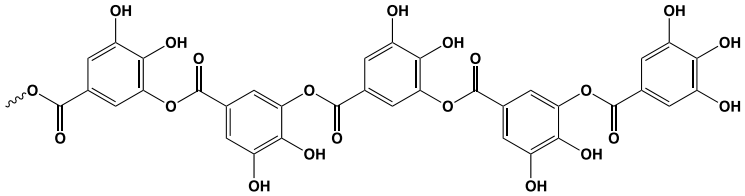


, or  .

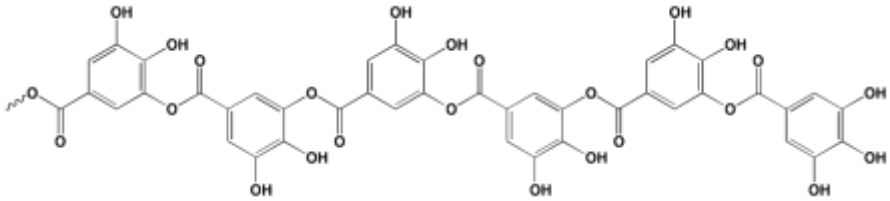
9. The use of claim 8, wherein each of R^1 and R^2, independently, is selected from the group consisting of:

 ,  ,  ,

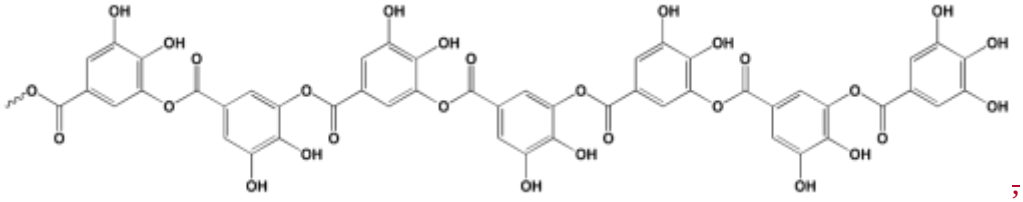
 ,



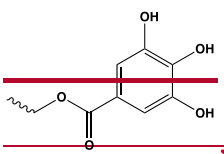
,



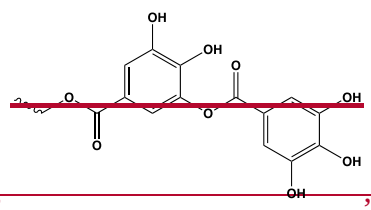
, and



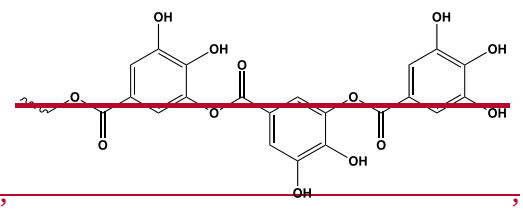
,



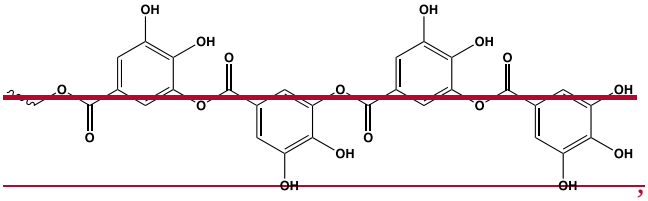
,



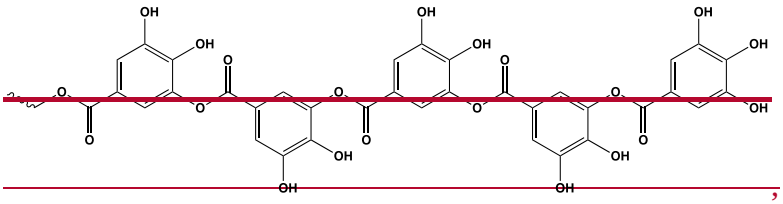
,



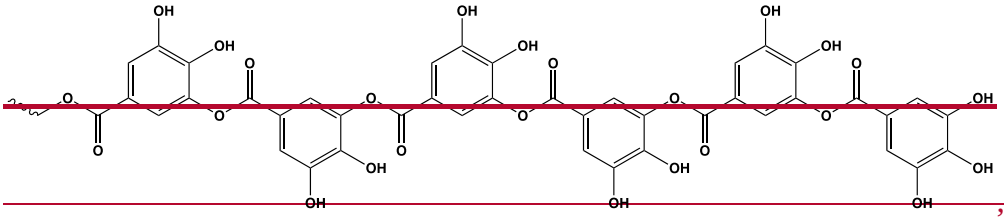
,



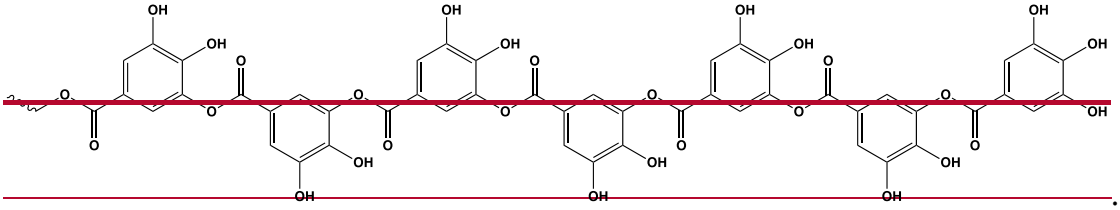
,



,



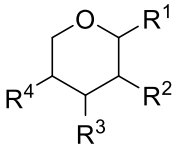
, and



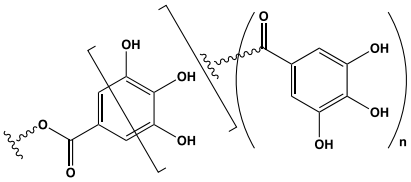
.

10. The use of claim 9, wherein the compound of Formula (If) is Resorcin 10G or Resorcin 14G.

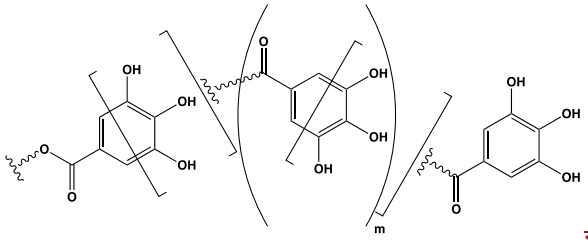
11. The use of claim 1, wherein the compound is of the Formula (Ig)

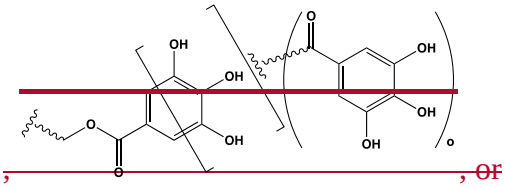


(Ig), in which each of R^1, R^2, R^3, and R^4, independently, is

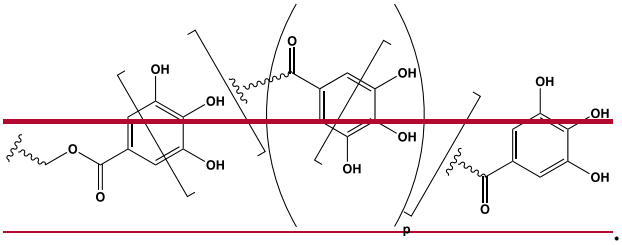


or,



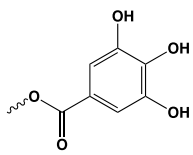
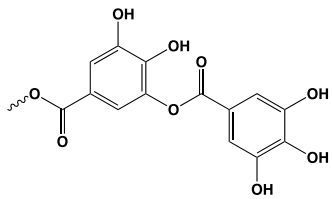
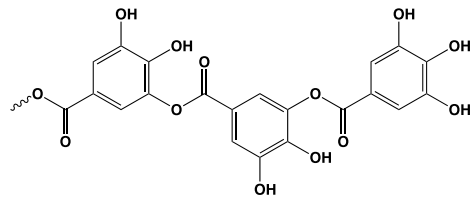


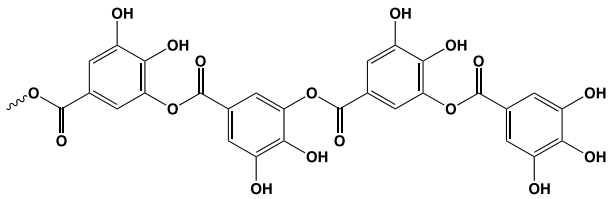
, or

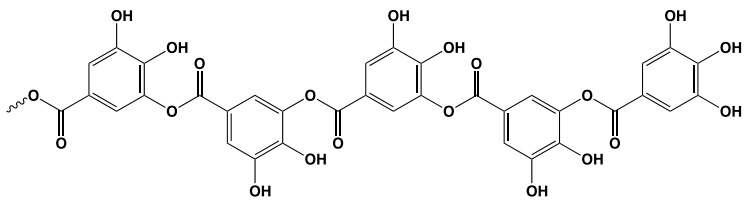


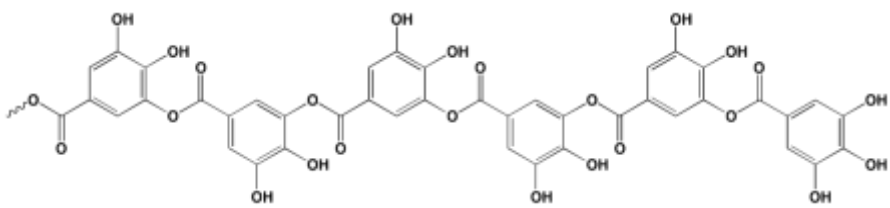
.

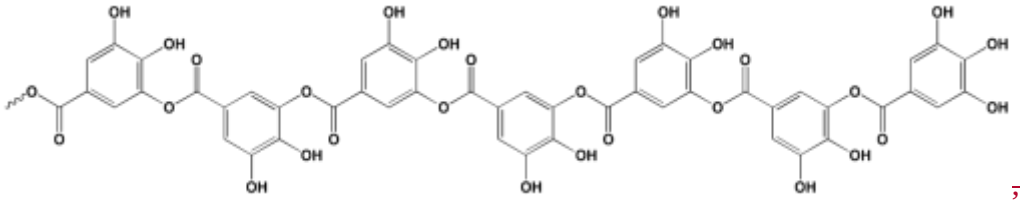
12. The use of claim 11, wherein each of R^1, R^2, R^3, and R^4, independently, is selected from the group consisting of:

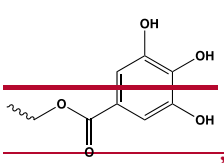
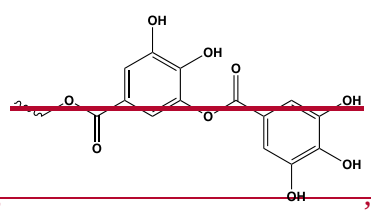
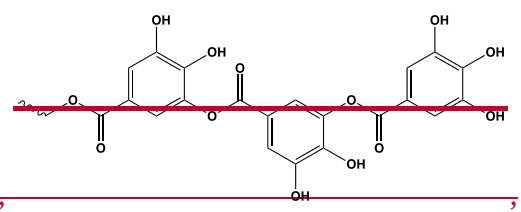
 ,  ,  ,

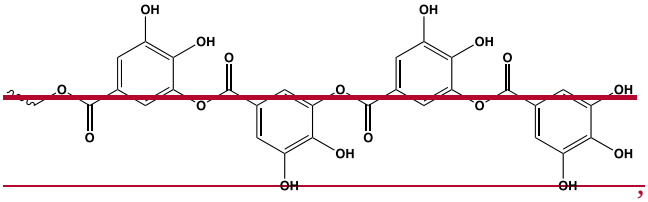
 ,

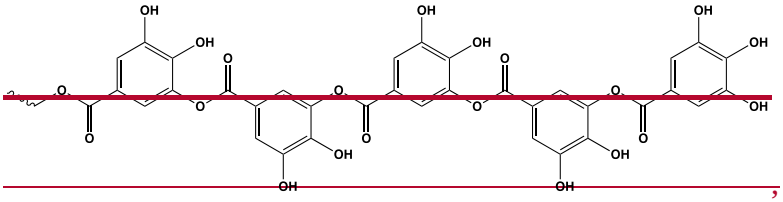
 ,

 , and

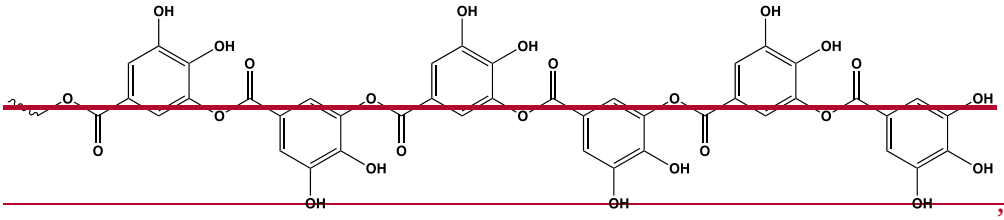
 ,

 ,  ,  ,

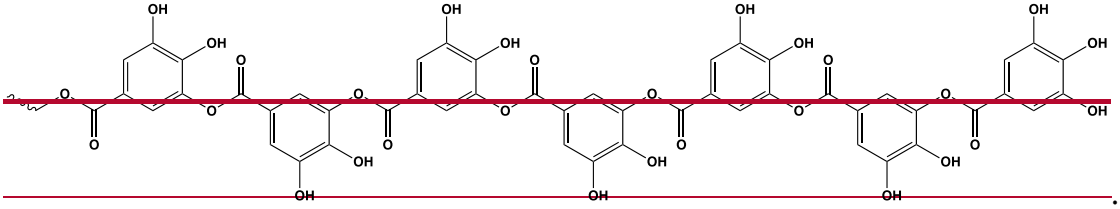
 ,



,



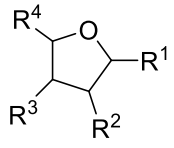
, and



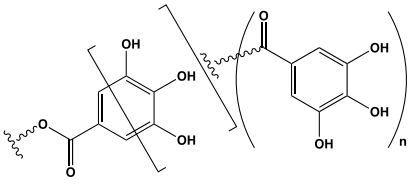
.

13. The use of claim 12, wherein the compound of Formula (Ig) is Compound 117, 119, 121, 123, 126, or 128.

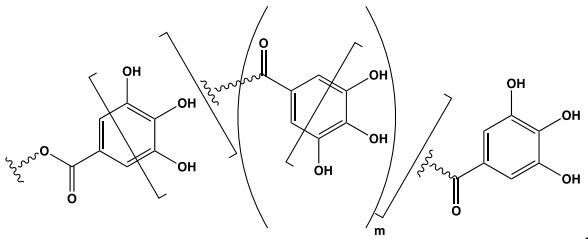
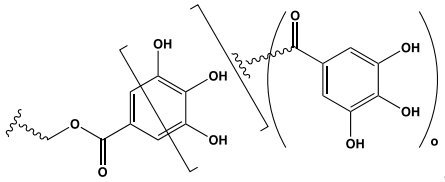
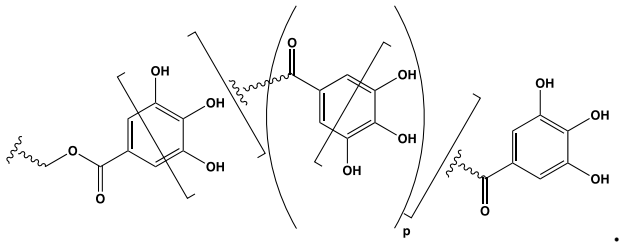
14. The use of claim 1, wherein the compound is of the Formula (Ih)



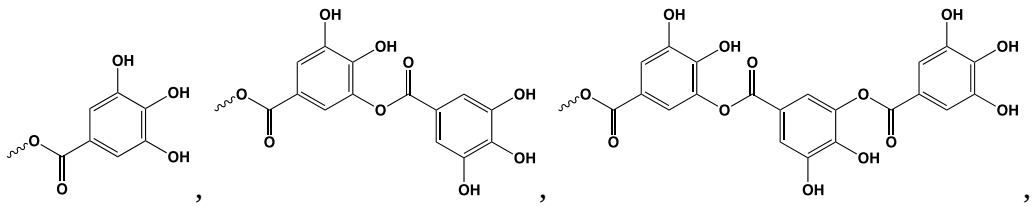
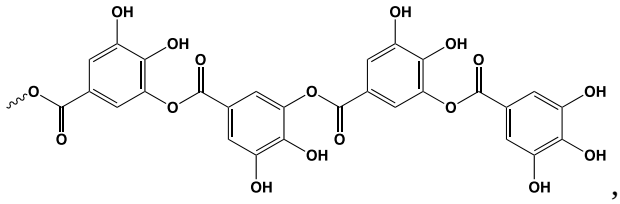
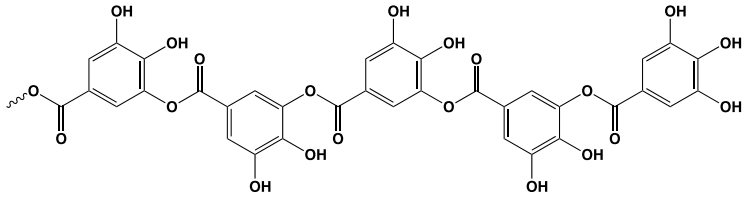
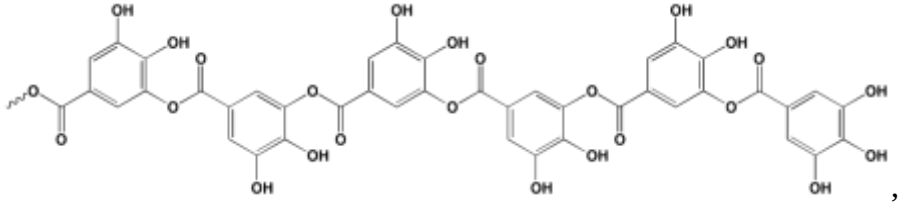
(Ih), in which each of R^1, R^2, R^3, and R^4, independently, is

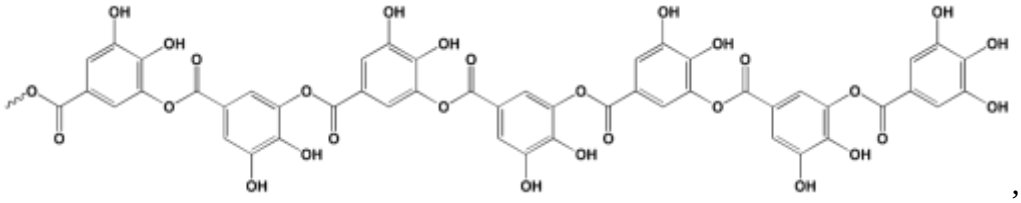
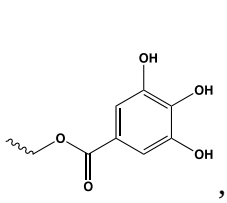
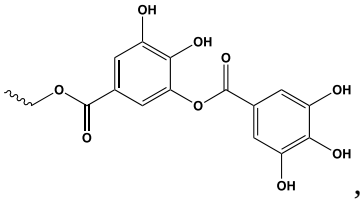
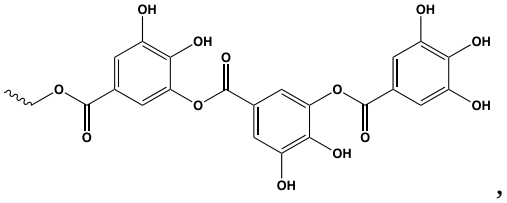
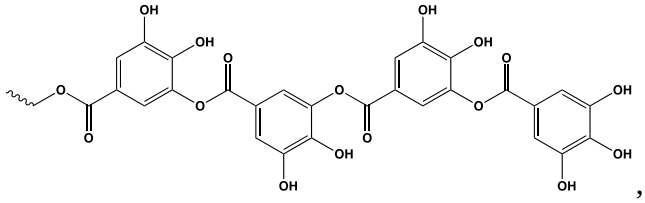
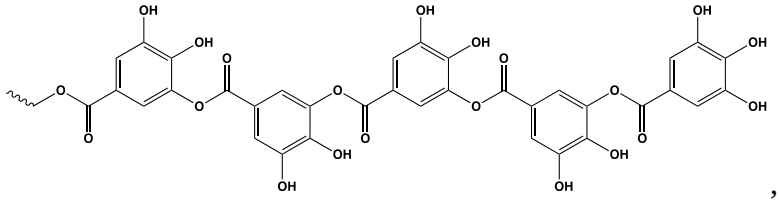
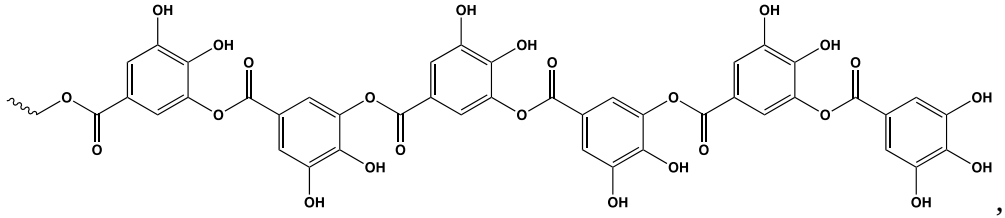
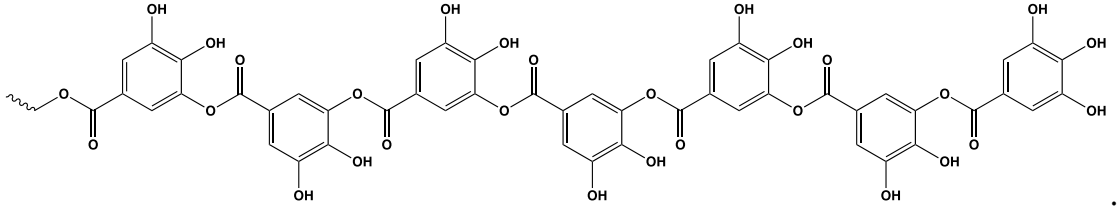


,


, 
, or 
.

15. The use of claim 14, wherein each of R^1, R^2, R^3, and R^4, independently, is selected from the group consisting of:


,
,
,

,

,

,


,

,

,

,

,

,

, and

.

16. The use of claim 15, wherein the compound of Formula (Ij) is Compound 134, 136, 138, 140, 142, 144, 146, or 148.

17. The use of claim 1, wherein the composition is a nutraceutical composition, a health food, or a medical food.

18. The use of claim 1, wherein the coronavirus infection is an infection caused by a coronavirus SARS-CoV-2.

19. The use of claim 1, wherein the composition is to be administered to ~~the~~ a subject by oral administration, by injection, by topical administration, or by inhalation.

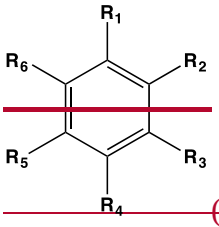
20. The use of claim 1, wherein the composition is placed in a medical device selected from the group consisting of an inhaler, a nebulizer, a nasal spray, and a vaporization aerosol device to be administered to ~~the~~ a subject.

21. The use of claim 19, wherein the subject is a human subject.

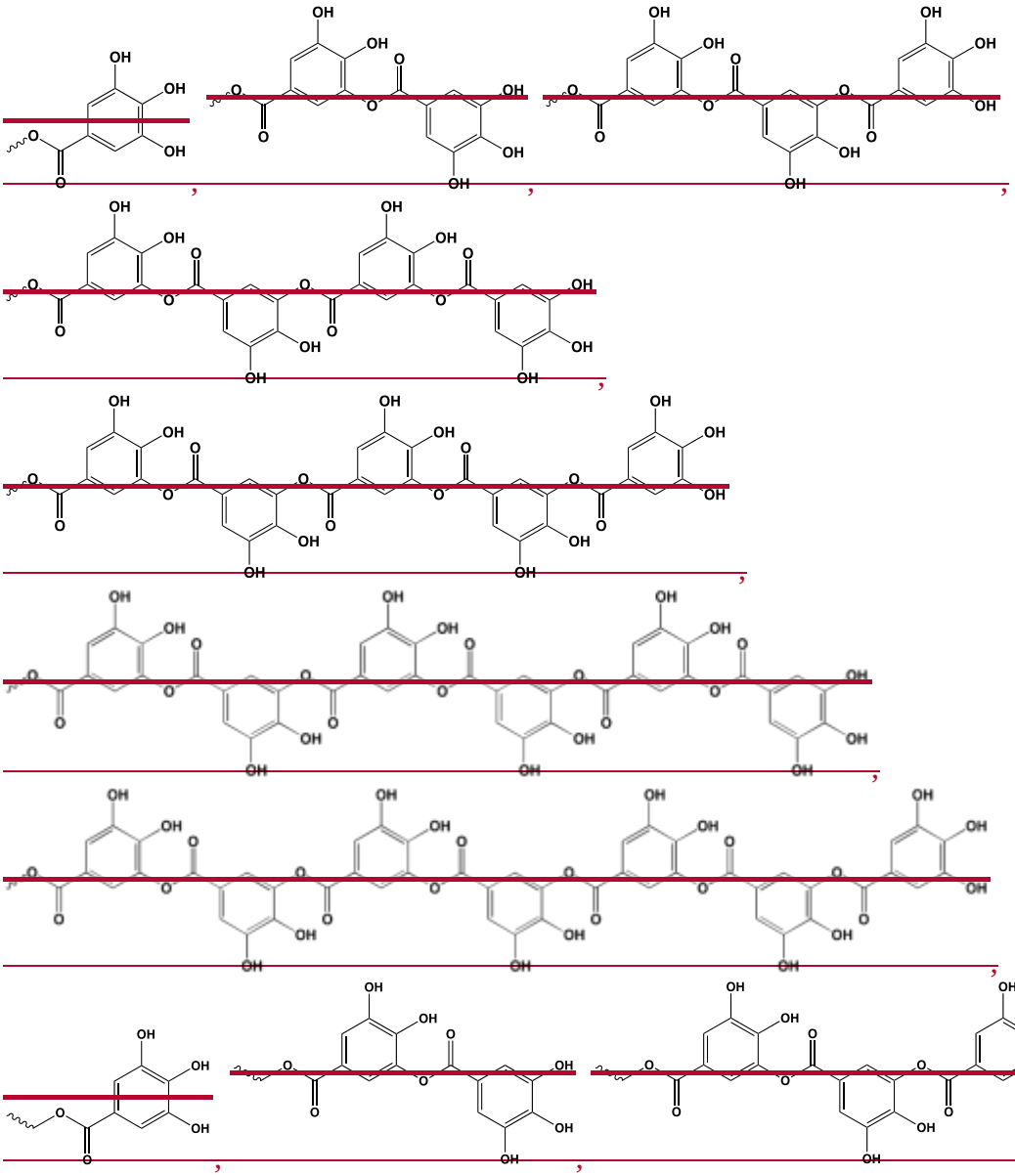
22. The use of claim 19, wherein the subject is to be administered the composition continuously or at a frequency of every five minutes to one time every three months.

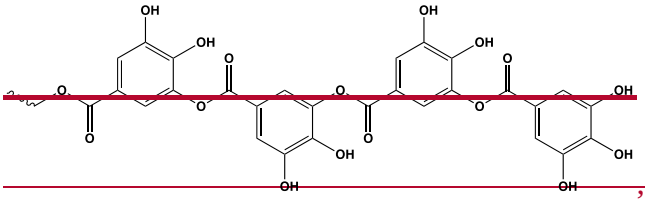
23. The use of claim 19, wherein the human subject is to be treated concurrently with, prior to, or subsequent to, one or more additional anti-viral agents.

24. The use of claim 1, wherein the compound is of the Formula (Ic)

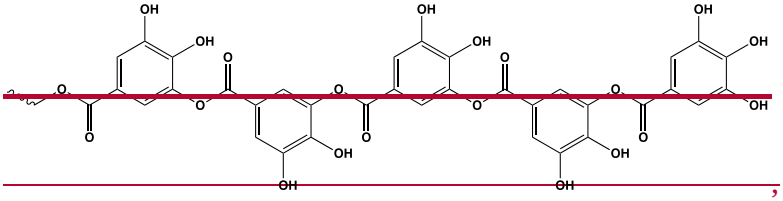


(Ic), in which R_1, R_2, R_3, R_4, R_5, and R_6 are each, independently, selected from the group consisting of:

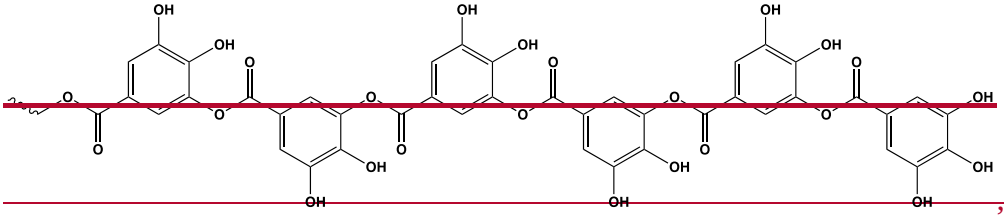




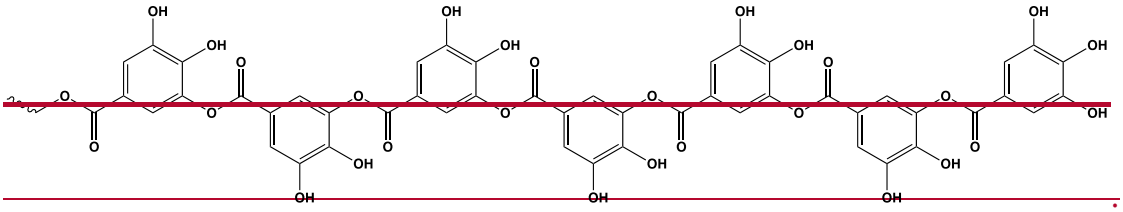
,



,



, and



.