

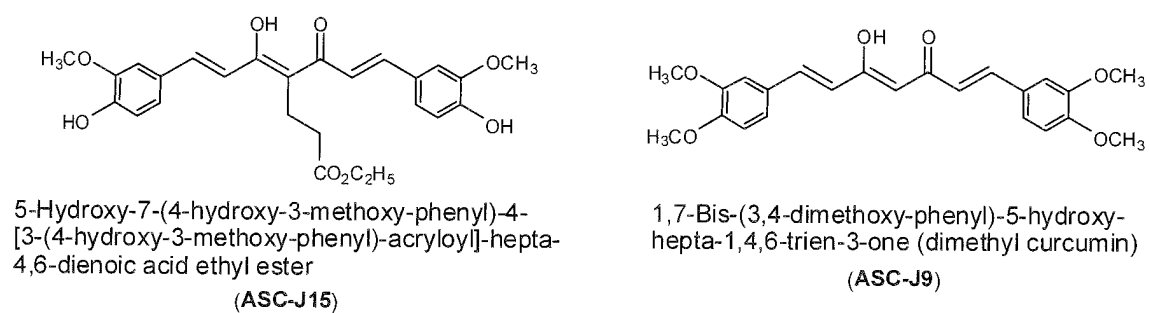


FIG. 1

## Summary of Select ASC compounds, structures and molecular weights.

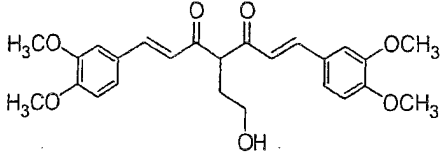
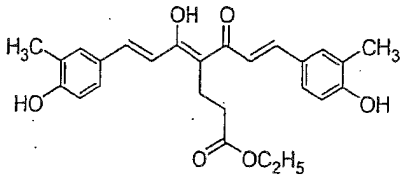
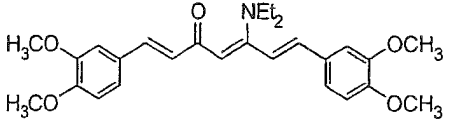
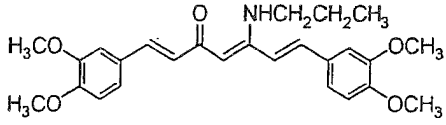
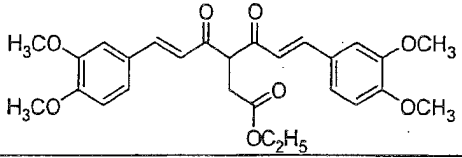
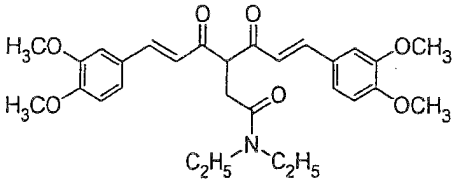
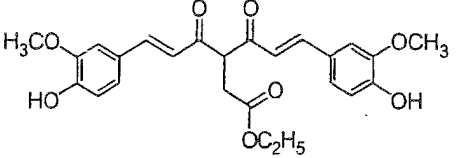
| Compound ID | Structure                                                                           | Formula<br>Molecular<br>weight |
|-------------|-------------------------------------------------------------------------------------|--------------------------------|
| ASC-Q9      |    | $C_{25}H_{28}O_7$<br>440.49    |
| ASC-Q12     |    | $C_{26}H_{28}O_6$<br>436.50    |
| ASC-Q30     |    | $C_{27}H_{33}NO_5$<br>451.55   |
| ASC-Q35     |   | $C_{26}H_{31}NO_5$<br>437.53   |
| ASC-Q44     |  | $C_{27}H_{30}O_8$<br>482.52    |
| ASC-Q49     |  | $C_{29}H_{35}NO_7$<br>509.59   |
| ASC-Q50     |  | $C_{25}H_{26}O_8$<br>454.47    |

FIG. 2A

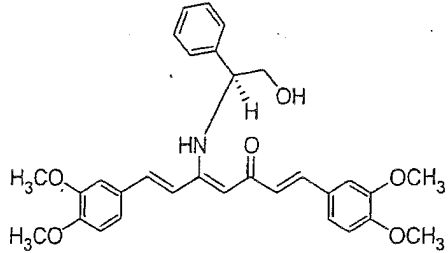
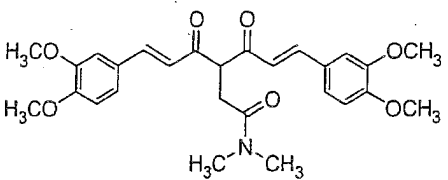
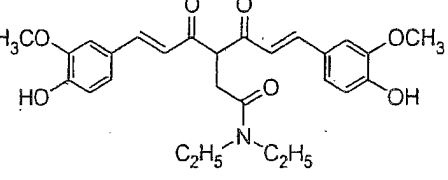
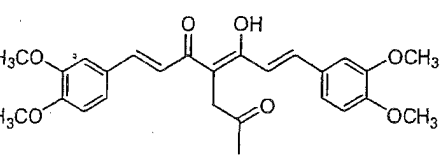
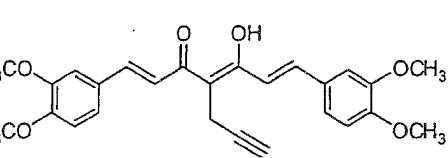
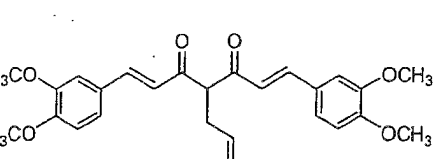
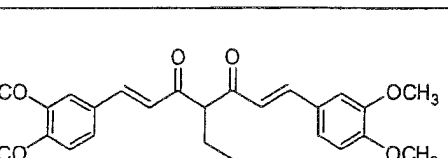
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|----------|--------------------------------------------------------------------------------------|------------------------------|
| ASC-Q70  |    | $C_{31}H_{33}NO_6$<br>515.60 |
| ASC-Q77  |    | $C_{27}H_{31}NO_7$<br>481.54 |
| ASC-Q98  |    | $C_{27}H_{31}NO_7$<br>481.54 |
| ASC-Q99  |   | $C_{26}H_{28}O_7$<br>452.50  |
| ASC-Q100 |  | $C_{26}H_{26}O_6$<br>434.48  |
| ASC-Q101 |  | $C_{26}H_{28}O_6$<br>436.50  |
| ASC-Q102 |  | $C_{25}H_{28}O_6$<br>424.49  |

FIG. 2B

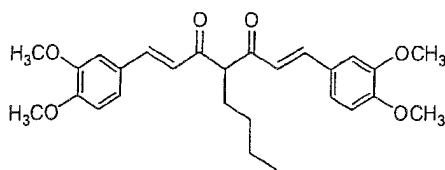
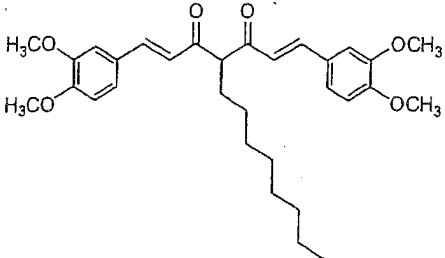
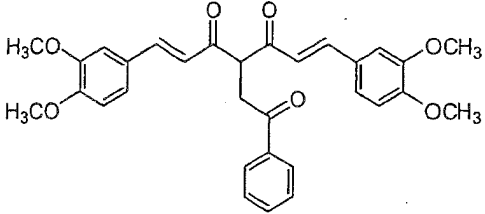
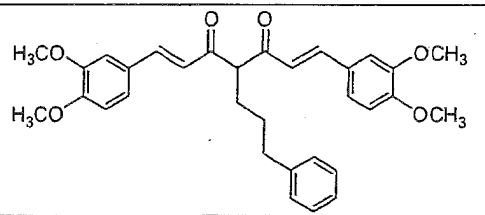
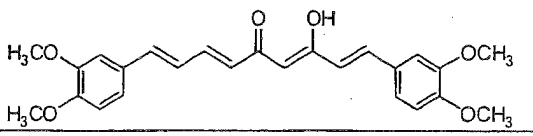
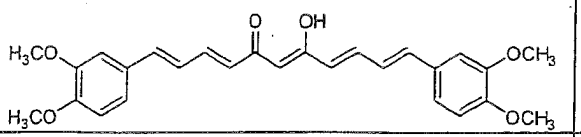
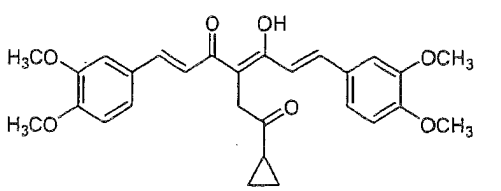
|          |                                                                                      |                             |
|----------|--------------------------------------------------------------------------------------|-----------------------------|
| ASC-Q103 |    | $C_{27}H_{32}O_6$<br>452.54 |
| ASC-Q104 |    | $C_{31}H_{40}O_6$<br>508.65 |
| ASC-Q106 |    | $C_{31}H_{30}O_7$<br>514.57 |
| ASC-Q108 |   | $C_{32}H_{34}O_6$<br>514.61 |
| ASC-Q110 |  | $C_{25}H_{26}O_6$<br>422.47 |
| ASC-Q111 |  | $C_{27}H_{28}O_6$<br>448.51 |
| ASC-Q113 |  | $C_{28}H_{30}O_7$<br>478.53 |

FIG. 2C

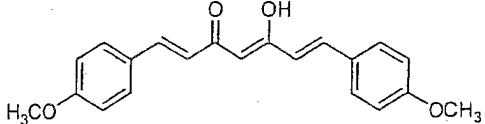
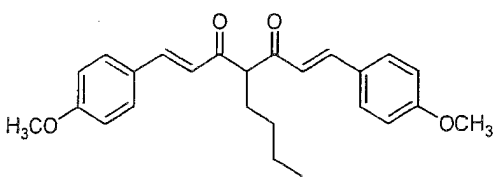
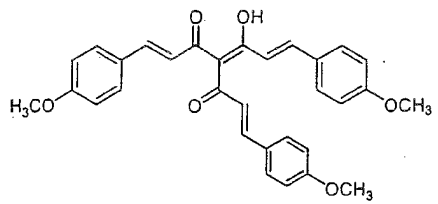
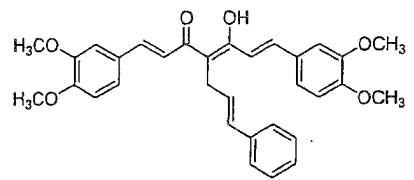
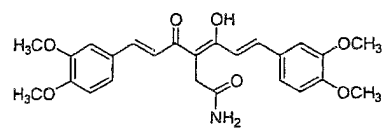
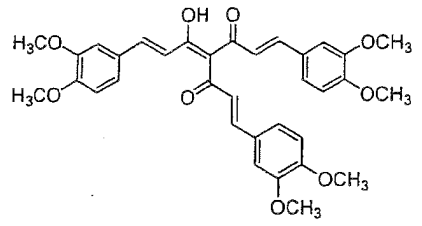
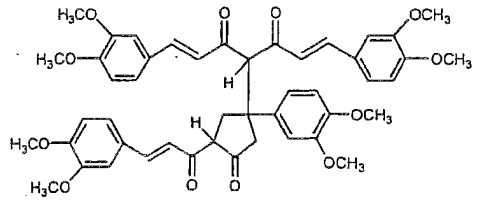
|          |                                                                                      |                                |
|----------|--------------------------------------------------------------------------------------|--------------------------------|
| ASC-Q114 |    | $C_{21}H_{20}O_4$<br>336.38    |
| ASC-Q115 |    | $C_{25}H_{28}O_4$<br>392.49    |
| ASC-Q116 |     | $C_{31}H_{28}O_6$<br>496.55    |
| ASC- JM1 |    | $C_{32}H_{32}O_6$<br>512.59    |
| ASC- JM2 |   | $C_{25}H_{27}NO_7$<br>453.48   |
| ASC- JM4 |   | $C_{34}H_{34}O_9$<br>586.63    |
| ASC-JM5  |  | $C_{47}H_{48}O_{12}$<br>804.87 |

FIG. 2D

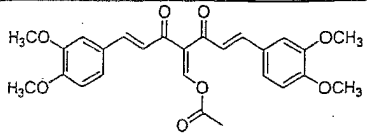
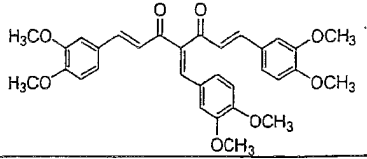
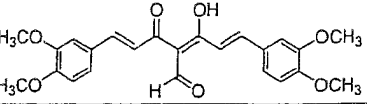
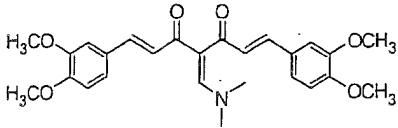
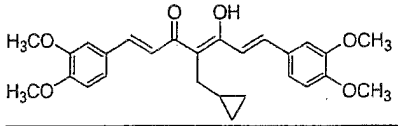
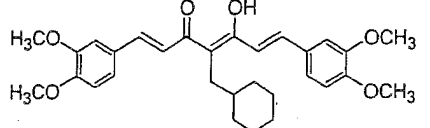
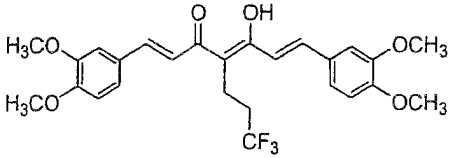
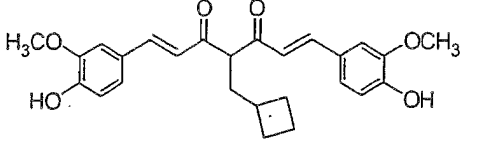
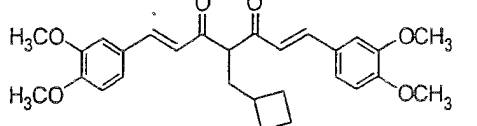
|           |                                                                                      |                                                                         |
|-----------|--------------------------------------------------------------------------------------|-------------------------------------------------------------------------|
| ASC- JM6  |     | C <sub>26</sub> H <sub>26</sub> O <sub>8</sub><br>466.48                |
| ASC- JM7  |     | C <sub>32</sub> H <sub>32</sub> O <sub>8</sub><br>544.59                |
| ASC- JM10 |     | C <sub>24</sub> H <sub>24</sub> O <sub>7</sub><br>424.44                |
| ASC- JM11 |     | C <sub>26</sub> H <sub>29</sub> NO <sub>6</sub><br>451.51               |
| ASC- JM12 |     | C <sub>27</sub> H <sub>30</sub> O <sub>6</sub><br>450.52                |
| ASC- JM13 |   | C <sub>30</sub> H <sub>36</sub> O <sub>6</sub><br>492.60                |
| ASC- JM14 |  | C <sub>26</sub> H <sub>27</sub> F <sub>3</sub> O <sub>6</sub><br>492.48 |
| ASC- JM16 |  | C <sub>26</sub> H <sub>28</sub> O <sub>6</sub><br>436.50                |
| ASC- JM17 |  | C <sub>28</sub> H <sub>32</sub> O <sub>6</sub><br>464.55                |

FIG. 2E

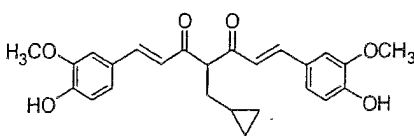
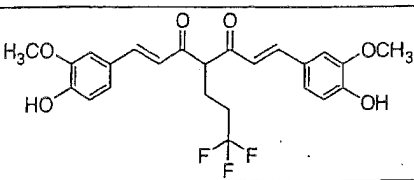
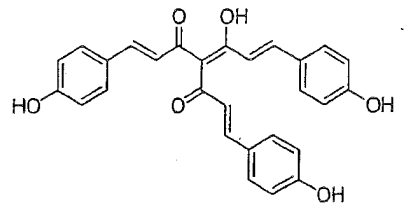
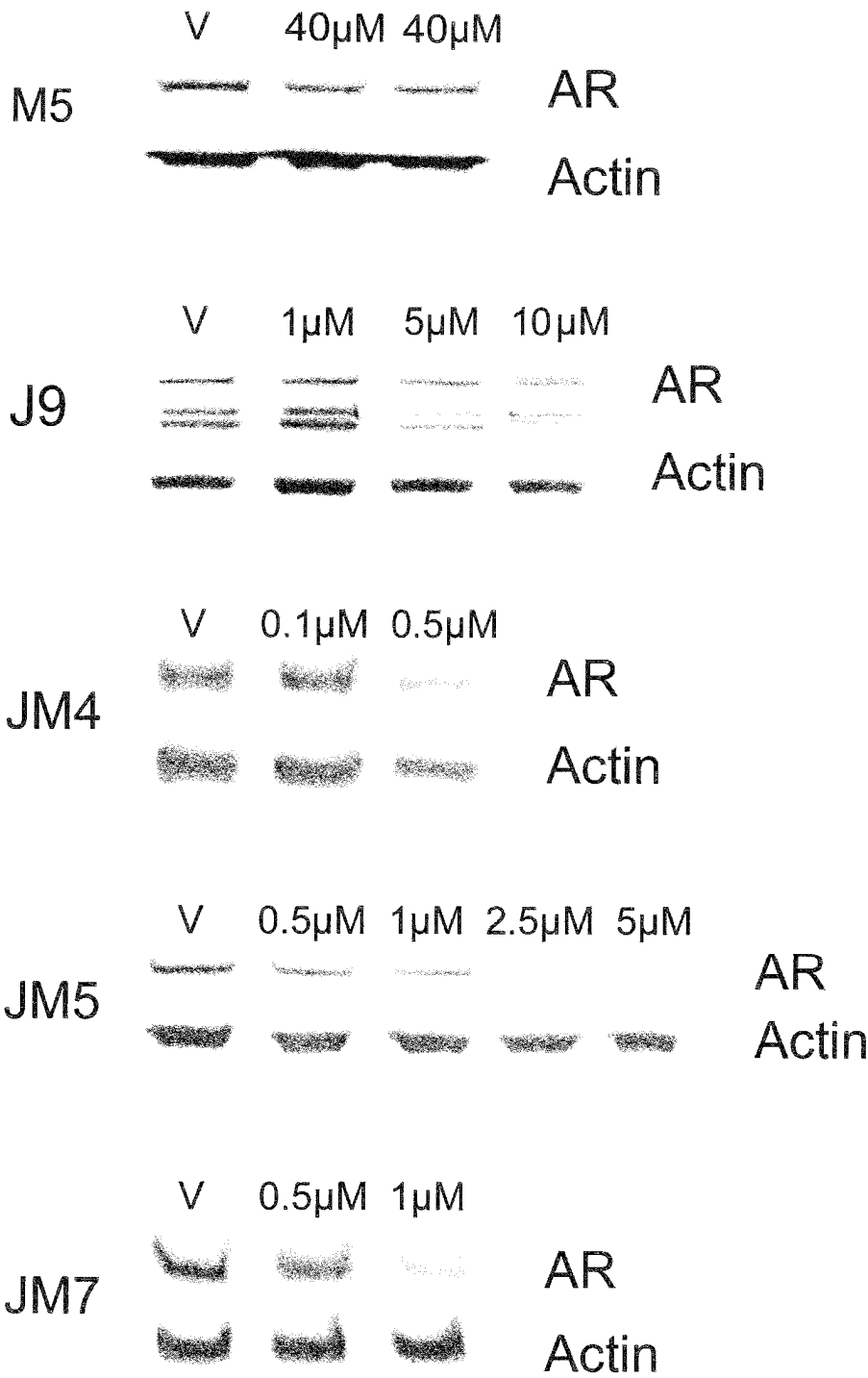
|           |                                                                                   |                                |
|-----------|-----------------------------------------------------------------------------------|--------------------------------|
| ASC- JM18 |  | $C_{25}H_{26}O_6$<br>422.47    |
| ASC- JM19 |  | $C_{24}H_{23}F_3O_6$<br>464.43 |
| ASC- JM20 |  | $C_{28}H_{22}O_6$<br>454.47    |

FIG. 2F

**FIG. 3. Compounds with (4-hydroxy-3-methoxy-phenyl)-propenal moieties reduce AR protein expression (% reduction) in prostate cancer CWR22Rv1 cells.**

| Treatment (concentration) | No. of moiety | 0.1 $\mu$ M | 0.5 $\mu$ M | 1.0 $\mu$ M | 2.5 $\mu$ M | 5.0 $\mu$ M | 40.0 $\mu$ M |
|---------------------------|---------------|-------------|-------------|-------------|-------------|-------------|--------------|
| Monomer-5                 | 1             |             |             |             |             | 0           | 37           |
| ASC-J9                    | 2             |             |             |             | 0           | 43          |              |
| ASC-JM4                   | 3             | 0           | 68          | 90          |             |             |              |
| ASC-JM5                   | 4             |             | 28          | 54          | 87          | 86          |              |
| ASC-JM7                   | 3             | 0           | 0           | 81          |             |             |              |

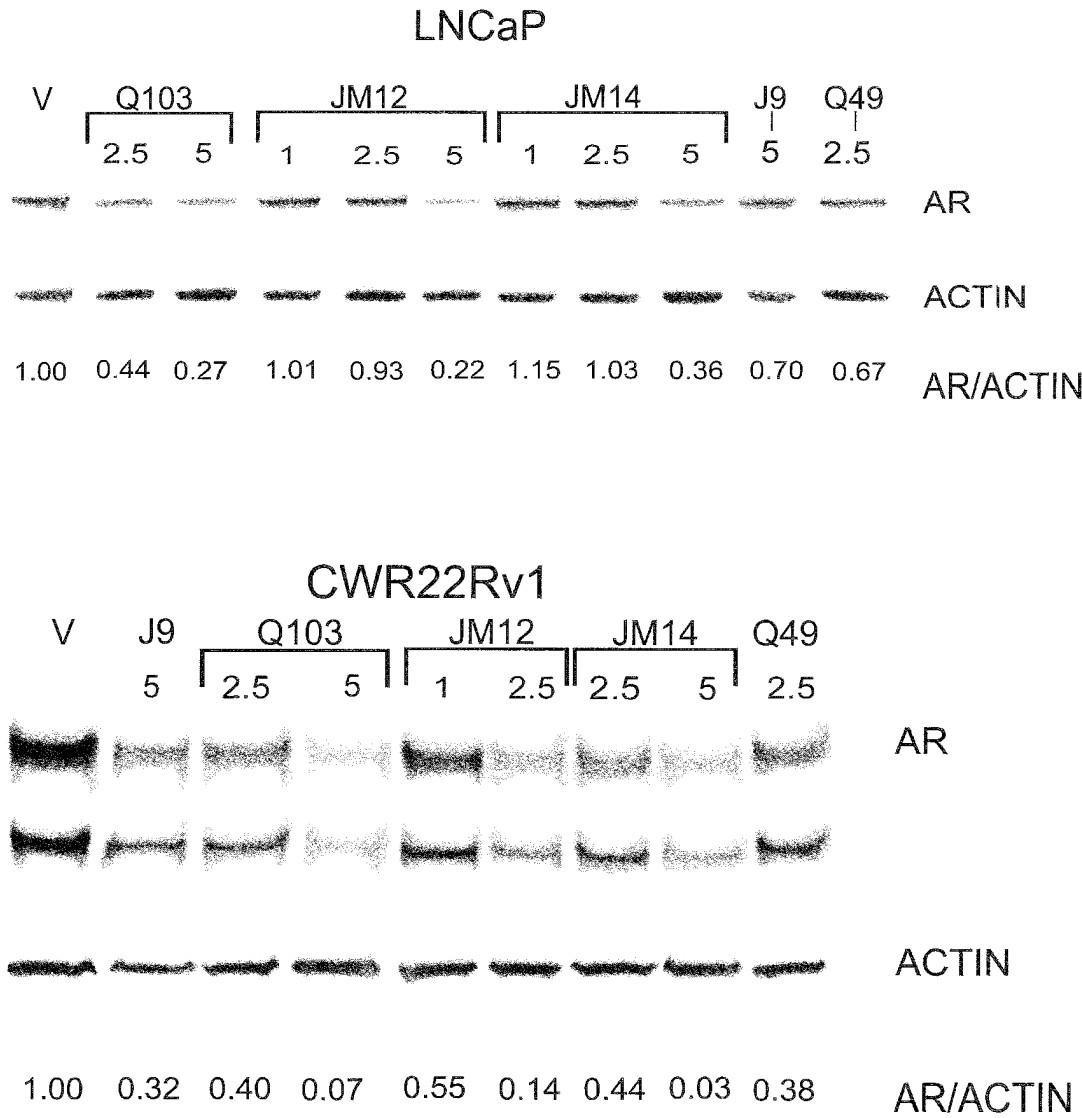
FIG. 4. Representative ASC compounds reduce AR protein expression.



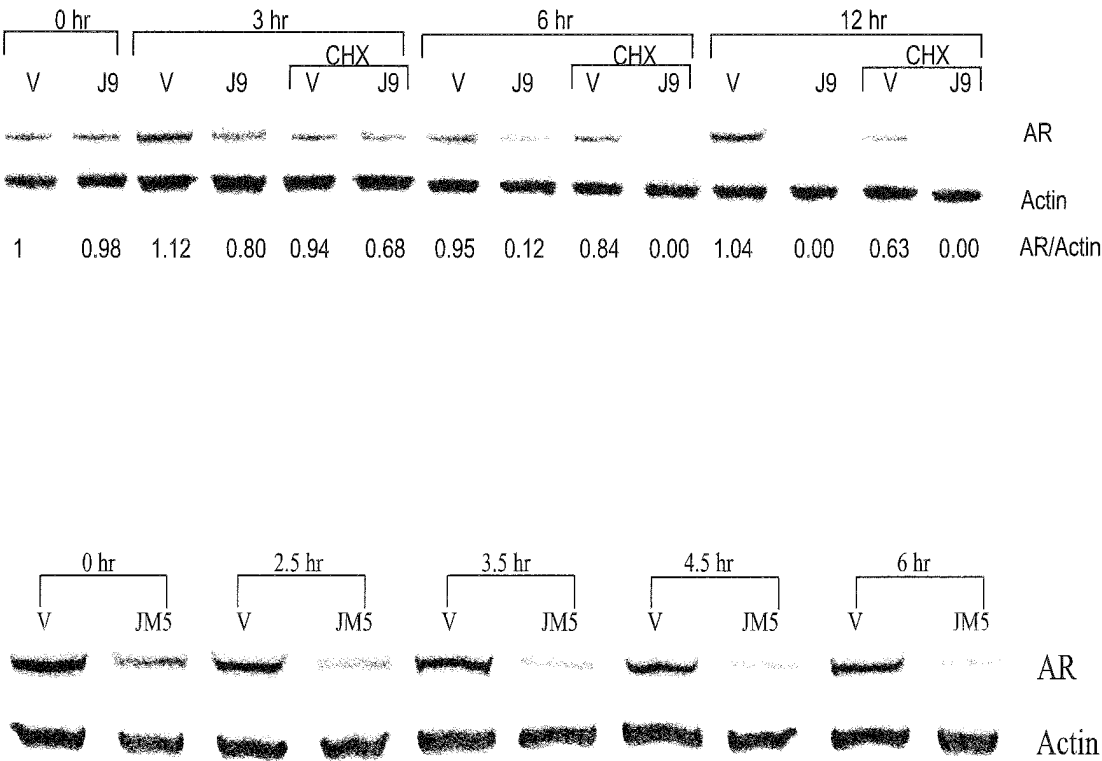
**FIG. 5. Representative ASC compounds inhibit prostate cancer cells (LNCaP and CWR22Rv1) growth *in vitro*.**

| Compound  | Inhibition of AR/DHT mediated cell growth |          |
|-----------|-------------------------------------------|----------|
|           | LNCaP                                     | CWR22rv1 |
| ASC-Q8    | +++                                       |          |
| ASC-Q9    | +++                                       |          |
| ASC-Q12   | ++                                        |          |
| ASC-Q30   | +++                                       |          |
| ASC-Q35   | ++                                        |          |
| ASC-Q44   | ++                                        |          |
| ASC-Q49   | ++                                        |          |
| ASC-Q50   | ++                                        |          |
| ASC-Q70   | +                                         |          |
| ASC-JM1   | ++                                        |          |
| ASC-JM4   | ++++                                      |          |
| ASC-JM5   | ++++                                      |          |
| ASC-JM6   | ++                                        |          |
| Monomer-1 |                                           | +        |
| Monomer-5 |                                           | ++       |

**FIG. 6. ASC-Q49, ASC-Q103, ASC-JM12, and ASC-JM4 compounds reduce AR protein expression in LNCaP and CWR22Rv1 cancer cells.**



**FIG. 7. ASC-J9 and ASC-JM5 enhance AR protein degradation in the presence of cycloheximide in LNCaP cells.**



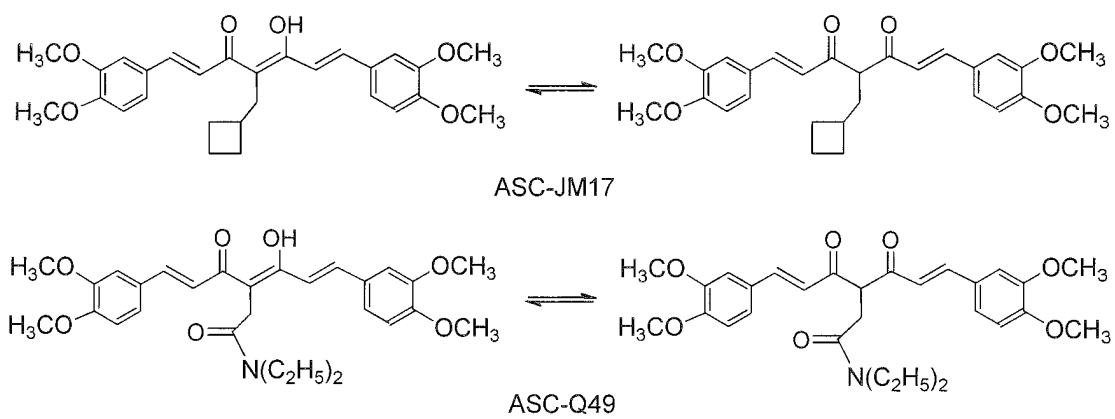
**FIG. 8. Representative ASC compounds reduce AR protein expression (% reduction) in LNCaP and CWR22Rv1 cells.**

Tested in LNCaP cells

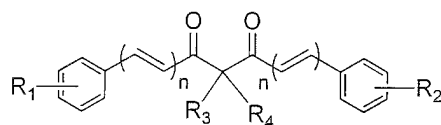
| Treatment | 1 $\mu$ M | 2.5 $\mu$ M | 5 $\mu$ M  | 7.5 $\mu$ M | 20 $\mu$ M | 40 $\mu$ M | Potency |
|-----------|-----------|-------------|------------|-------------|------------|------------|---------|
| ASC-Q101  |           | 4           | 47         |             |            |            | ++      |
| ASC-Q102  | 0         | 15          | cell death |             |            |            | +++     |
| ASC-Q103  | 0         | 48          | 73         |             |            |            | ++++    |
| ASC-Q104  |           |             | 27         | 56          |            |            | ++      |
| ASC-Q106  |           | 0           | 6          | 52          |            |            | +       |
| ASC-Q108  |           | 0           | 14         | 49          |            |            | +       |
| ASC-Q110  | 0         | 0*          | 58         | cell death  |            |            | ++      |
| ASC-Q111  |           |             | 50         | 62          |            |            | ++      |
| ASC-Q113  | 0         | 11          | cell death |             |            |            | +++     |
| ASC-Q116  |           | 0           | 30         | 68          |            |            | ++      |
| ASC-JM12  | 5         | 22          | 81         |             |            |            | ++++    |
| ASC-JM13  |           | 0           | 43         | 76          |            |            | ++      |
| ASC-JM14  | 0         | 21          | 74         |             |            |            | ++++    |

Tested in CWR22Rv1 cells

| Treatment | 1 $\mu$ M | 2.5 $\mu$ M | 5 $\mu$ M  | 7.5 $\mu$ M | 20 $\mu$ M | 40 $\mu$ M | Potency |
|-----------|-----------|-------------|------------|-------------|------------|------------|---------|
| ASC-Q101  |           | 0           | 53         |             |            |            | ++      |
| ASC-Q103  | 8         | 49          | 93         |             |            |            | ++++    |
| ASC-Q113  | 0         | 28          | cell death |             |            |            | +++     |
| ASC-Q116  |           | 77          | cell death |             |            |            | ++++    |
| ASC-JM12  | 36        | 71          |            |             |            |            | ++++    |
| ASC-JM13  |           | 15          | 40         | 87          |            |            | ++      |
| ASC-JM14  | 0         | 43          | 95         |             |            |            | ++++    |

**FIG. 9.** Tautomers of ASC-JM17 and ASC-Q49

**FIG. 10A.** Summary of representative compounds including 4,4-disubstituted 1,7-bis-(3,4-dimethoxyphenyl)-hepta-1,6-diene-3,5-dione and 6,6-disubstituted 1,11-bis(substituted phenyl)-undeca-1,3,8,10-tetraene-5,7-dione scaffolds.



| Compound ID | R <sub>1</sub>         | R <sub>2</sub>        | R <sub>3</sub>                                  | R <sub>4</sub>  | n | formula                                                                   |
|-------------|------------------------|-----------------------|-------------------------------------------------|-----------------|---|---------------------------------------------------------------------------|
| 1           | 3'4'-OCH <sub>3</sub>  | 3'4'-OCH <sub>3</sub> | CH <sub>2</sub> -                               | CH <sub>3</sub> | 1 | C <sub>28</sub> H <sub>32</sub> O <sub>6</sub><br>464.55                  |
| 2           | 3'4'-OCH <sub>3</sub>  | 3'4'-OCH <sub>3</sub> | CH <sub>2</sub> -                               | CH <sub>3</sub> | 1 | C <sub>29</sub> H <sub>34</sub> O <sub>6</sub><br>478.5767                |
| 3           | 3'4'-OCH <sub>3</sub>  | 3'4'-OCH <sub>3</sub> | CH <sub>2</sub> -                               | H               | 1 | C <sub>29</sub> H <sub>34</sub> O <sub>6</sub><br>478.58                  |
| 4           | 3'4'-OCH <sub>3</sub>  | 3'4'-OCH <sub>3</sub> | CH <sub>2</sub> -                               | CH <sub>3</sub> | 1 | C <sub>30</sub> H <sub>36</sub> O <sub>6</sub><br>492.60                  |
| 5           | 3'4'-OCH <sub>3</sub>  | 3'4'-OCH <sub>3</sub> | CH <sub>2</sub> -                               | CH <sub>3</sub> | 1 | C <sub>31</sub> H <sub>38</sub> O <sub>6</sub><br>506.63                  |
| 6           | 3'4'-OCH <sub>3</sub>  | 3'4'-OCH <sub>3</sub> | CH <sub>2</sub> -                               | CH <sub>3</sub> | 1 | C <sub>30</sub> H <sub>37</sub> NO <sub>7</sub><br>523.62                 |
| 7           | 3'4'-OCH <sub>3</sub>  | 3'4'-OCH <sub>3</sub> | CH <sub>2</sub> -                               | CH <sub>3</sub> | 1 | C <sub>28</sub> H <sub>33</sub> NO <sub>7</sub><br>495.56                 |
| 8           | 3'4'-OCH <sub>3</sub>  | 3'4'-OCH <sub>3</sub> | (CH <sub>2</sub> ) <sub>3</sub> CH <sub>3</sub> | CH <sub>3</sub> | 1 | C <sub>28</sub> H <sub>34</sub> O <sub>6</sub><br>466.57                  |
| 9           | 3'4'-OCH <sub>3</sub>  | 3'4'-OCH <sub>3</sub> | CH <sub>2</sub> -                               | H               | 1 | C <sub>29</sub> H <sub>33</sub> NO <sub>8</sub><br>523.57                 |
| 10          | 3'4'-OCH <sub>3</sub>  | 3'4'-OCH <sub>3</sub> | CH <sub>2</sub> -                               | H               | 1 | C <sub>28</sub> H <sub>28</sub> N <sub>2</sub> O <sub>7</sub> S<br>536.60 |
| 11          | 3'4'-CH <sub>3</sub>   | 3'4'-CH <sub>3</sub>  | CH <sub>2</sub> -                               | CH <sub>3</sub> | 1 | C <sub>30</sub> H <sub>35</sub> NO <sub>8</sub><br>537.60                 |
| 12          | 3'4'-OCH <sub>3</sub>  | 3'4'-OCH <sub>3</sub> | CH <sub>2</sub> -                               | CH <sub>3</sub> | 1 | C <sub>29</sub> H <sub>30</sub> N <sub>2</sub> O <sub>7</sub> S<br>550.62 |
| 13          | 3'4'-OCH <sub>3</sub>  | 3'4'-OCH <sub>3</sub> | CH <sub>2</sub> -                               | F               | 1 | C <sub>27</sub> H <sub>29</sub> FO <sub>6</sub><br>468.51                 |
| 14          | 3'4'-OOCH <sub>3</sub> | 3'4'-OCH <sub>3</sub> | CH <sub>2</sub> -                               | F               | 1 | C <sub>28</sub> H <sub>31</sub> FO <sub>6</sub><br>482.54                 |
| 15          | 3'4'-OCH <sub>3</sub>  | 3'4'-OCH <sub>3</sub> | CH <sub>2</sub> -                               | F               | 1 | C <sub>29</sub> H <sub>33</sub> FO <sub>6</sub><br>496.57                 |

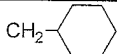
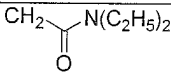
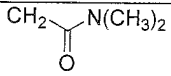
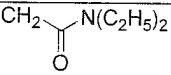
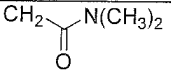
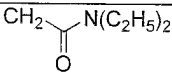
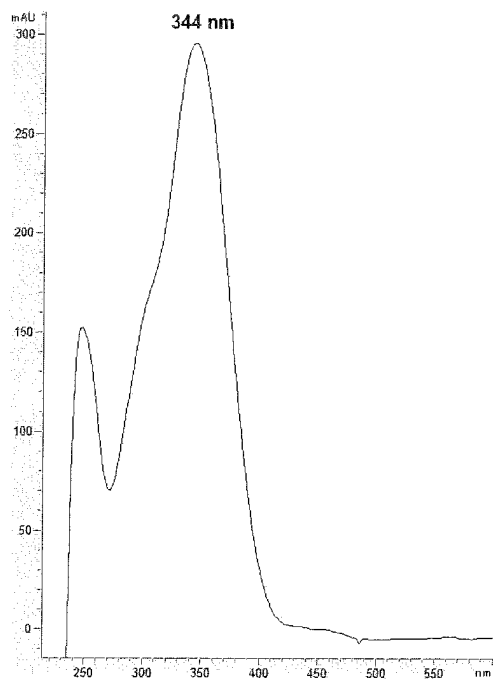
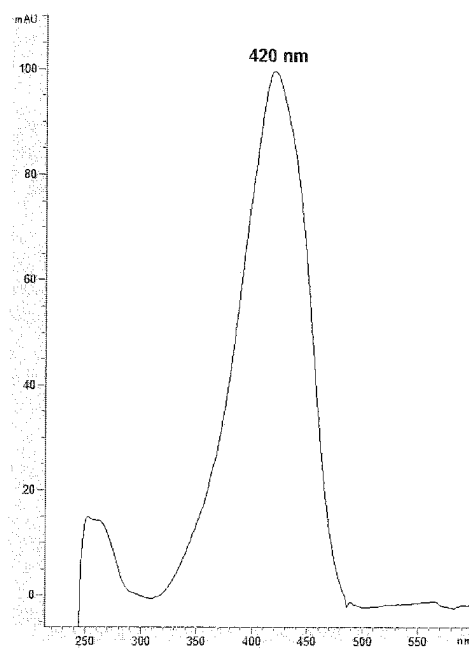
|    |                                                   |                                                   |                                                                                     |                 |   |                                                                         |
|----|---------------------------------------------------|---------------------------------------------------|-------------------------------------------------------------------------------------|-----------------|---|-------------------------------------------------------------------------|
| 16 | 3'4'-OCH <sub>3</sub>                             | 3'4'-OCH <sub>3</sub>                             |    | F               | 1 | C <sub>30</sub> H <sub>35</sub> FO <sub>6</sub><br>510.59               |
| 17 | 3'4'-OCH <sub>3</sub>                             | 3'4'-OCH <sub>3</sub>                             |   | F               | 1 | C <sub>29</sub> H <sub>34</sub> FNO <sub>7</sub><br>527.58              |
| 18 | 3'4'-OCH <sub>3</sub>                             | 3'4'-OCH <sub>3</sub>                             |   | F               | 1 | C <sub>27</sub> H <sub>30</sub> FNO <sub>7</sub><br>499.53              |
| 19 | 3'4'-OCH <sub>3</sub>                             | 3'4'-OCH <sub>3</sub>                             | (CH <sub>2</sub> ) <sub>3</sub> CH <sub>3</sub>                                     | F               | 1 | C <sub>27</sub> H <sub>31</sub> FO <sub>6</sub><br>470.53               |
| 20 | 3'4'-OCH <sub>3</sub>                             | 3'4'-OCH <sub>3</sub>                             |   | Cl              | 1 | C <sub>29</sub> H <sub>34</sub> ClNO <sub>7</sub><br>544.04             |
| 21 | 3'4'-OCH <sub>3</sub>                             | 3'4'-OCH <sub>3</sub>                             |   | Cl              | 1 | C <sub>27</sub> H <sub>30</sub> ClNO <sub>7</sub><br>515.98             |
| 22 | 3'4'-OCH <sub>3</sub>                             | 3'4'-OCH <sub>3</sub>                             | CH <sub>2</sub> CH <sub>2</sub> COOC <sub>2</sub> H <sub>5</sub>                    | CH <sub>3</sub> | 1 | C <sub>29</sub> H <sub>34</sub> O <sub>8</sub><br>510.58                |
| 23 | 3'4'-OCH <sub>3</sub>                             | 3'4'-OCH <sub>3</sub>                             | CH <sub>2</sub> CH <sub>2</sub> COOC <sub>2</sub> H <sub>5</sub>                    | F               | 1 | C <sub>28</sub> H <sub>31</sub> FO <sub>8</sub><br>514.54               |
| 24 | 3'4'-OCH <sub>3</sub>                             | 3'4'-OCH <sub>3</sub>                             | CH <sub>2</sub> CH <sub>2</sub> COOH                                                | CH <sub>3</sub> | 1 | C <sub>27</sub> H <sub>30</sub> O <sub>8</sub><br>482.52                |
| 25 | 3'4'-OCH <sub>3</sub>                             | 3'4'-OCH <sub>3</sub>                             | CH <sub>2</sub> CH <sub>2</sub> COOH                                                | F               | 1 | C <sub>26</sub> H <sub>27</sub> FO <sub>8</sub><br>486.49               |
| 26 | 3'OCH <sub>3</sub> ,4'OH                          | 3'OCH <sub>3</sub> ,4'OH                          | CH <sub>2</sub> CH <sub>2</sub> COOC <sub>2</sub> H <sub>5</sub>                    | CH <sub>3</sub> | 1 | C <sub>27</sub> H <sub>30</sub> O <sub>8</sub><br>482.52                |
| 27 | 3'OCH <sub>3</sub> ,4'OH                          | 3'OCH <sub>3</sub> ,4'OH                          | CH <sub>2</sub> CH <sub>2</sub> COOC <sub>2</sub> H <sub>5</sub>                    | F               | 1 | C <sub>26</sub> H <sub>27</sub> FO <sub>8</sub><br>486.49               |
| 28 | 3'-OCH <sub>3</sub>                               | 3'-OCH <sub>3</sub>                               |  | CH <sub>3</sub> |   | C <sub>27</sub> H <sub>30</sub> O <sub>4</sub><br>418.52                |
| 29 | 3'-OH                                             | 3'-OH                                             |  | CH <sub>3</sub> | 1 | C <sub>25</sub> H <sub>26</sub> O <sub>4</sub><br>390.47                |
| 30 | 3'-OCH <sub>3</sub>                               | 3'-OSO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> |  | CH <sub>3</sub> | 1 | C <sub>28</sub> H <sub>32</sub> O <sub>6</sub> S<br>496.62              |
| 31 | 3'-OSO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> | 3'-OSO <sub>2</sub> C <sub>2</sub> H <sub>5</sub> |  | CH <sub>3</sub> | 1 | C <sub>29</sub> H <sub>34</sub> O <sub>8</sub> S <sub>2</sub><br>574.71 |
| 32 | 3'4'-OCH <sub>3</sub>                             | 3'4'-OCH <sub>3</sub>                             |  | CH <sub>3</sub> | 2 | C <sub>34</sub> H <sub>41</sub> NO <sub>7</sub><br>575.69               |
| 33 | 3'4'-OCH <sub>3</sub>                             | 3'4'-OCH <sub>3</sub>                             |  | F               | 2 | C <sub>32</sub> H <sub>35</sub> FO <sub>6</sub><br>534.62               |

FIG. 10B

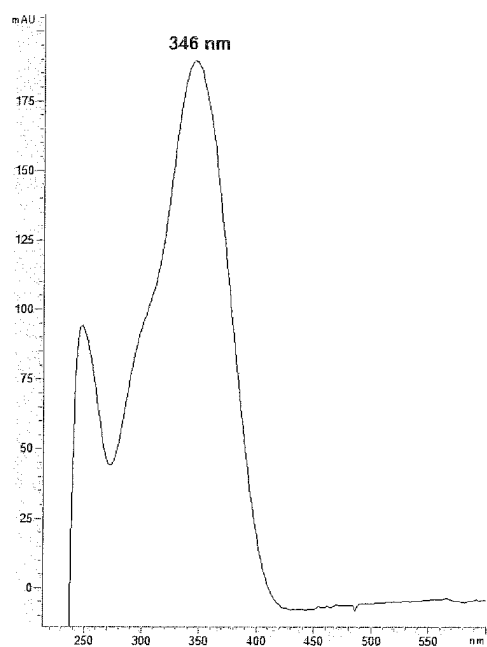
**FIG. 11:** UV spectra of ASC-Q49: diketone tautomer peak (**FIG. 11A**, RT 20.6 minutes), enol tautomer peak (**FIG. 11B**, RT 23.7 minutes), and compound **6** (**FIG. 11C**, RT 21.1 minutes).



A



B



C