

## **Supplementary file**

### **In Vitro and Randomized Controlled Clinical Study of Natural Constituents' Anti-HPV Potential for Treatment of Plantar Warts Supported with In Silico Studies and Network Analysis**

Nourhan Hisham Shady <sup>1,2,†</sup>, Fatma Alzahraa Mokhtar <sup>3,4,†</sup>, Hend Samy Abdullah <sup>5</sup>, Salah A. Abdel-Aziz <sup>6,7</sup>, Soad A. Mohamad <sup>8</sup>, Mohamed S. Imam <sup>9,10,\*</sup>, Sherin Refat El Afify <sup>11</sup> and Usama Ramadan Abdelmohsen <sup>1,12,\*</sup>

<sup>1</sup> Department of Pharmacognosy, Faculty of Pharmacy, Deraya University, Universities Zone, New Minia 61111, Egypt; norhan.shady@deraya.edu.eg

<sup>2</sup> Center for Research and Sustainability, Deraya University, Universities Zone, New Minia 61111, Egypt

<sup>3</sup> Fujairah Research Centre, Sakamkam Road, Sakamkam, Fujairah 0000, United Arab Emirates; drfatmaalzahraa1950@gmail.com

<sup>4</sup> Department of Pharmacognosy, Faculty of Pharmacy, El Saleheya El Gadida University, El Saleheya El Gadida, Sharkia 44813, Egypt

<sup>5</sup> Faculty of Pharmacy, Deraya University, Universities Zone, New Minia City 61111, Egypt; hend.samy\_1180443@student.deraya.edu.eg

<sup>6</sup> Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Deraya University, Universities Zone, New Minia 61111, Egypt; salah.abdelaziz@deraya.edu.eg

<sup>7</sup> Department of Pharmaceutical Medicinal Chemistry, Faculty of Pharmacy, Al-Azhar University, Assiut 71524, Egypt

<sup>8</sup> Department of Clinical Pharmacy, Faculty of Pharmacy, Deraya University, Universities Zone, New Minia 61111, Egypt; soad.ali@deraya.edu.eg

<sup>9</sup> Department of Clinical Pharmacy, College of Pharmacy, Shaqra University, Shaqra 11961, Saudi Arabia

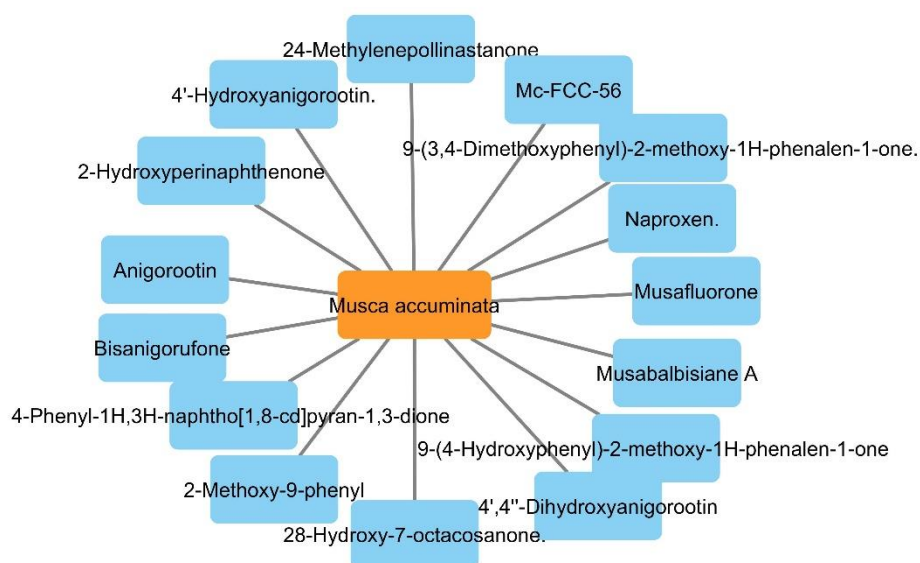
<sup>10</sup> Department of Clinical Pharmacy, National Cancer Institute, Cairo University, Fom El Khalig Square, Kasr Al-Aini Street, Cairo 11796, Egypt

<sup>11</sup> Department of Pharmacology and Toxicology, Faculty of Pharmacy, Alsalam University, Kafr alZayat, Algharbia 31611, Egypt; sherinelafify@gmail.com

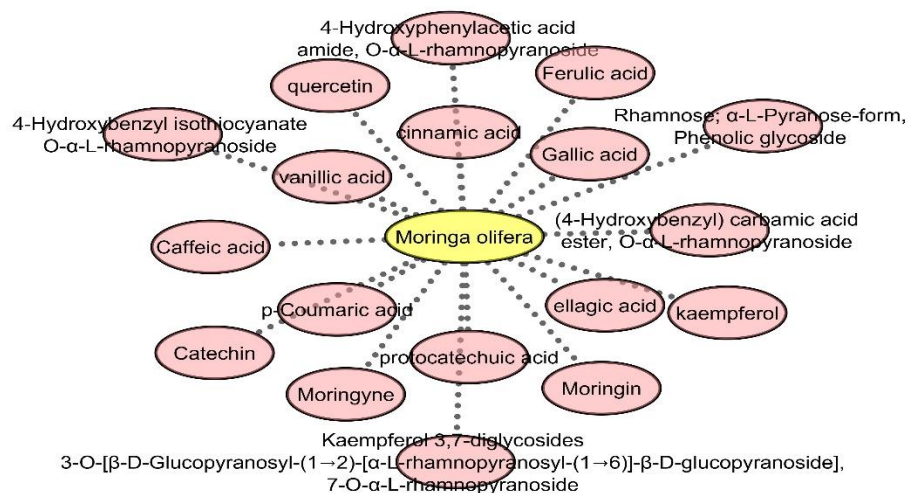
<sup>12</sup> Department of Pharmacognosy, Faculty of Pharmacy, Minia University, Minia 61519, Egypt

\* Correspondence: imammohamed311@gmail.com (M.S.I.); usama.ramadan@mu.edu.eg (U.R.A.)

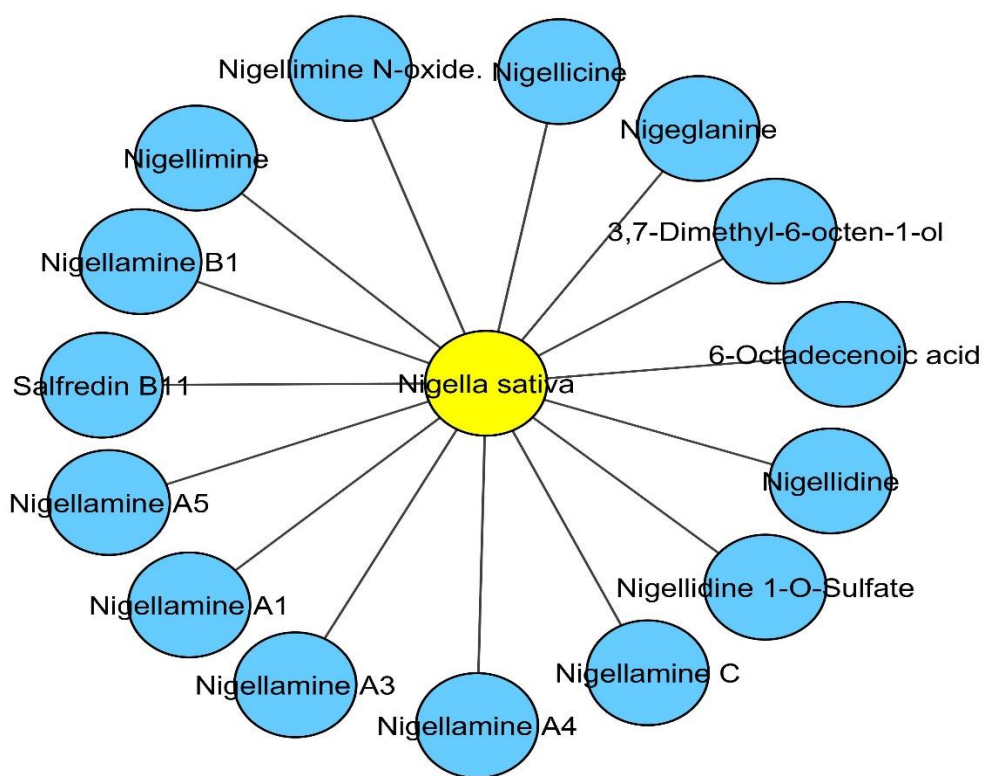
† These authors contributed equally to this work.



**Figure S1:** *Musca accuminata*-compounds Network; a network connecting the plant *Musca accuminata* (in orange rectangle) to the identified compounds (in blue rectangles)

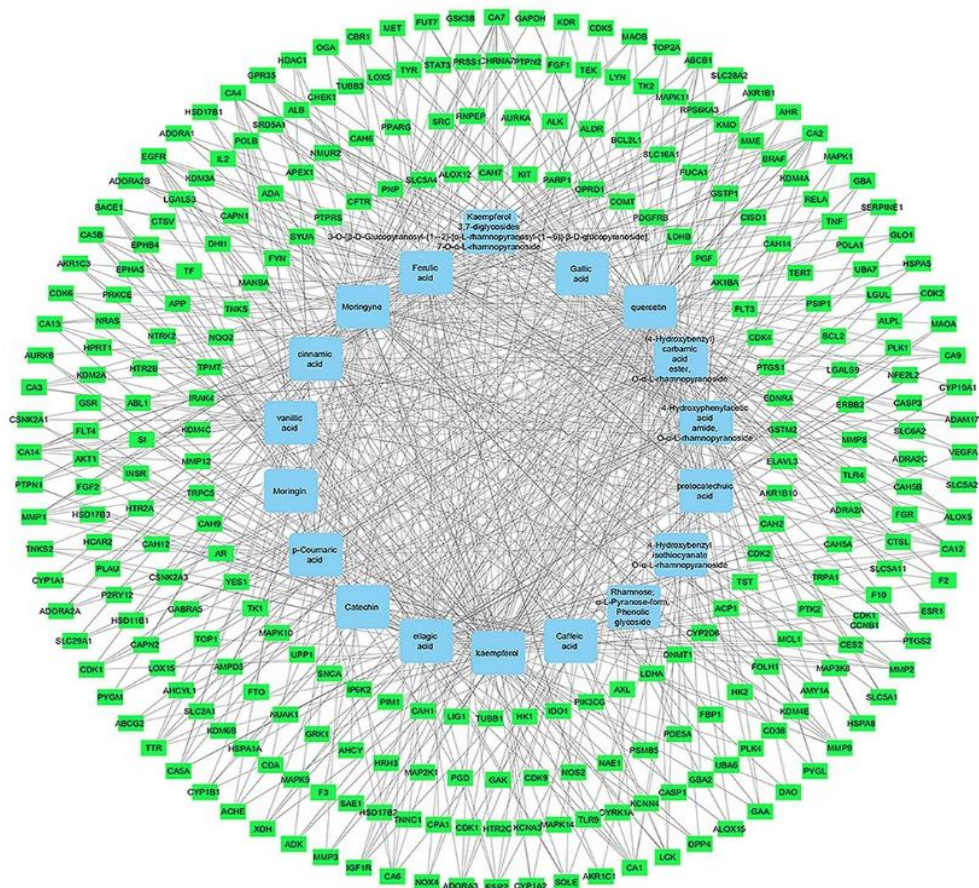


**Figure S2:** *Moringa olifera*-compounds Network; a network connecting the plant *Moringa olifera* (in yellow oval shape) to the identified compounds (in pink oval shapes)

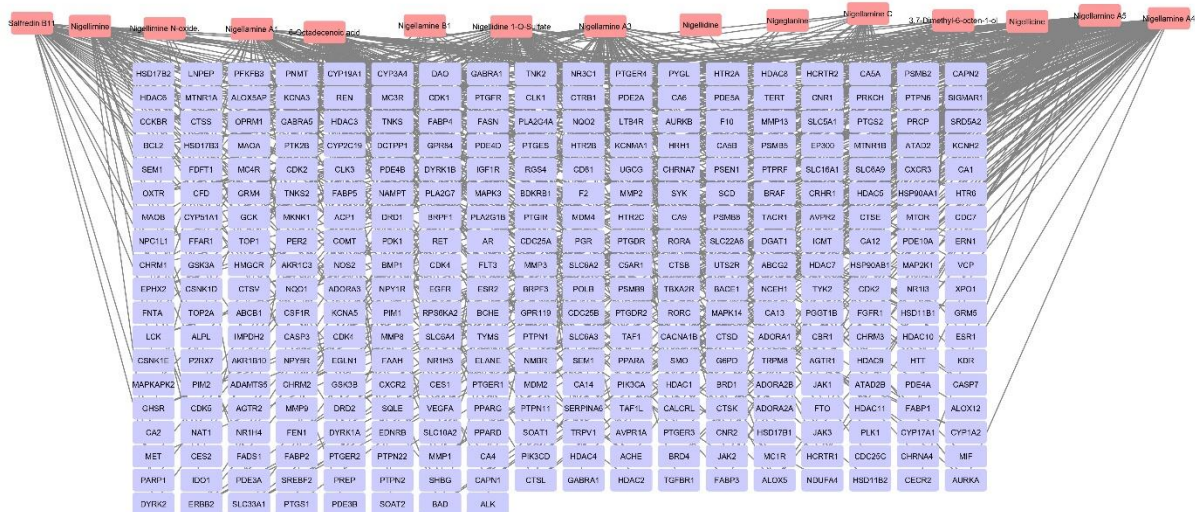


**Figure S3:** *Nigella sativa*-compounds Network; a network connecting the plant *Nigella sativa* (in yellow circle) to the identified compounds (in blue circles)



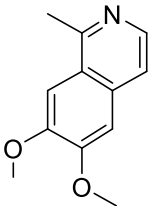
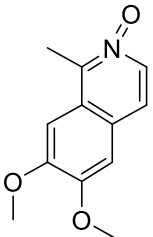
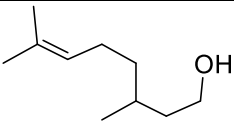
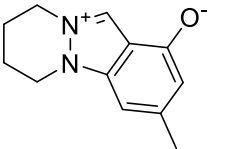
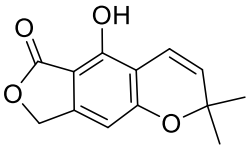
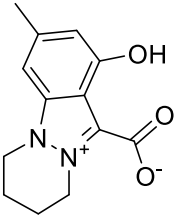


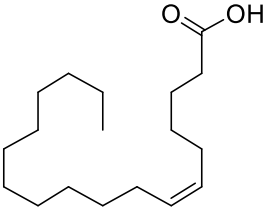
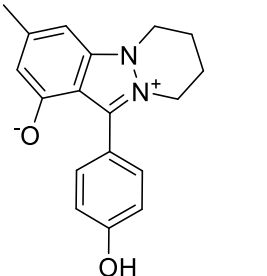
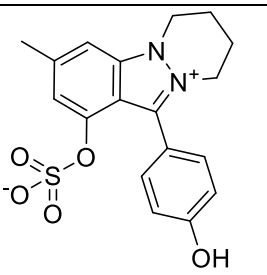
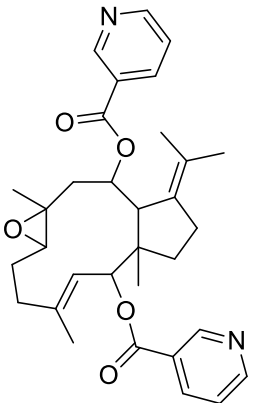
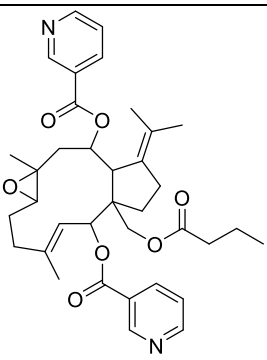
**Figure S5:** *Moringa olifera* compounds-targets network: a network describing the identified compounds from *Moringa olifera* (in blue rectangles) to their target genes (in green rectangles)

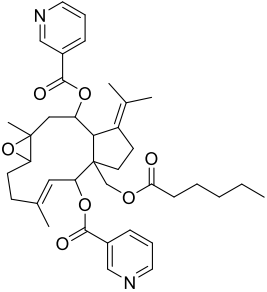
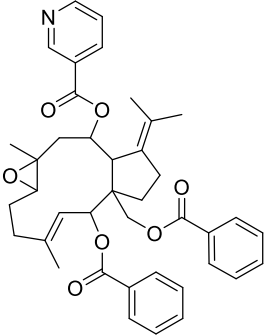
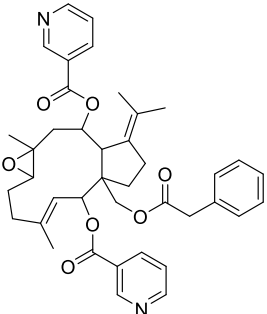
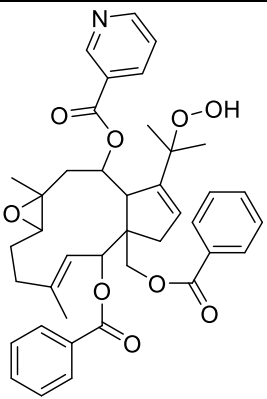


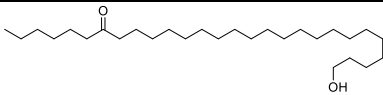
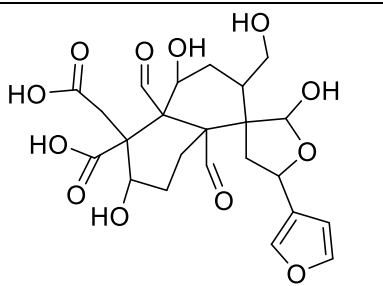
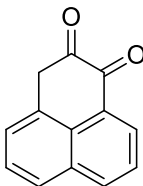
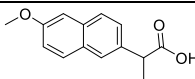
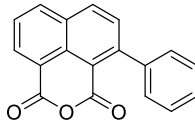
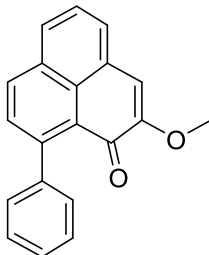
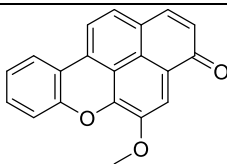
**Figure S6:** Nigella compounds-targets network, a merged network illustrates the identified compounds from *Nigella sativa* (in pink rectangles) to their targets (in violet rectangles)

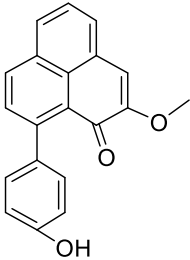
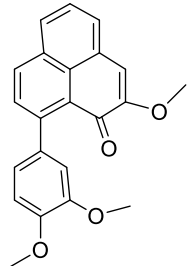
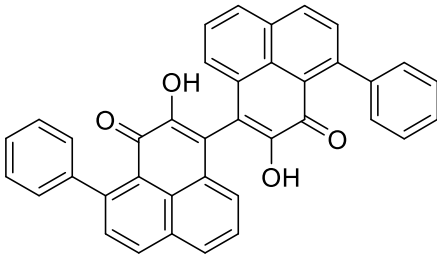
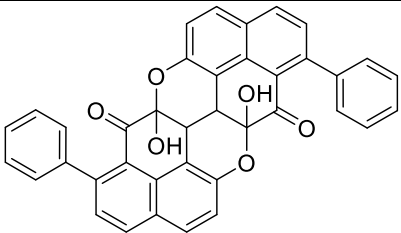
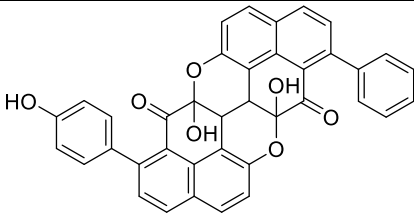
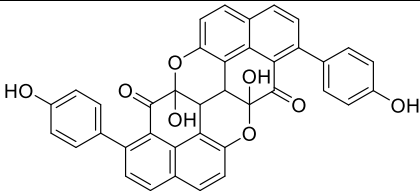
**Table S1:** LC-MS Assisted Dereplication of the Chemical Constituents in *Nigella sativa* seed, *Musca accuminata* peels and *Moringa olifera* seed extracts.

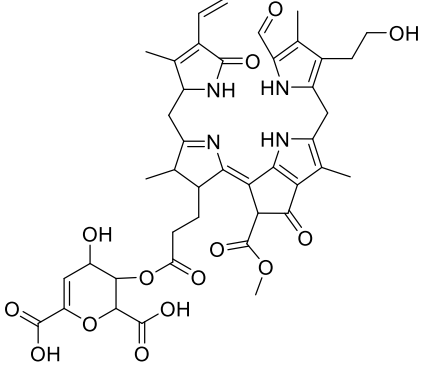
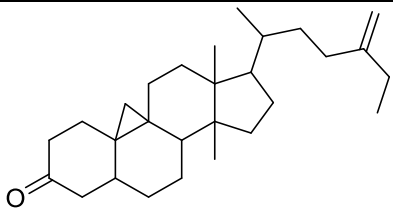
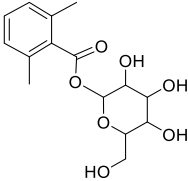
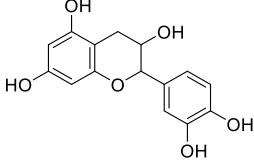
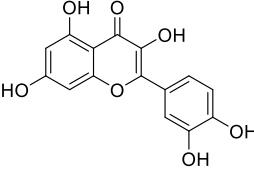
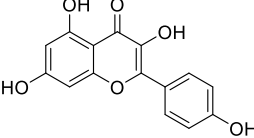
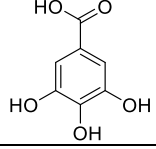
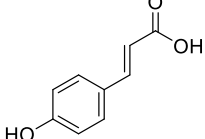
| No | Name                         | structure                                                                           | Exact mass     | Molecular formula                                             | Reference |
|----|------------------------------|-------------------------------------------------------------------------------------|----------------|---------------------------------------------------------------|-----------|
| 1  | Nigellimine                  |    | 203.0946<br>29 | C <sub>12</sub> H <sub>13</sub> NO <sub>2</sub>               | [1]       |
| 2  | Nigellimine<br>N-oxide.      |    | 219.0895<br>44 | C <sub>12</sub> H <sub>13</sub> NO <sub>3</sub>               | [2]       |
| 3  | 3,7-Dimethyl-6-octen-1-ol.   |  | 156.1514<br>15 | C <sub>10</sub> H <sub>20</sub> O                             | [3]       |
| 4  | Nigeglanine                  |  | 202.1106<br>13 | C <sub>12</sub> H <sub>14</sub> NO                            | [4]       |
| 5  | Salfredin<br>B <sub>11</sub> |  | 232.0735<br>6  | C <sub>13</sub> H <sub>12</sub> O <sub>4</sub>                | [5]       |
| 6  | Nigellicine                  |  | 246.1004<br>43 | C <sub>13</sub> H <sub>14</sub> N <sub>2</sub> O <sub>3</sub> | [6]       |

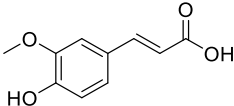
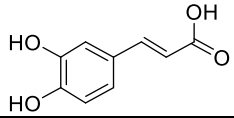
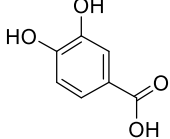
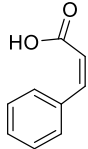
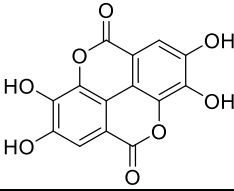
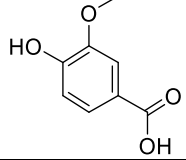
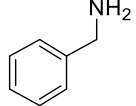
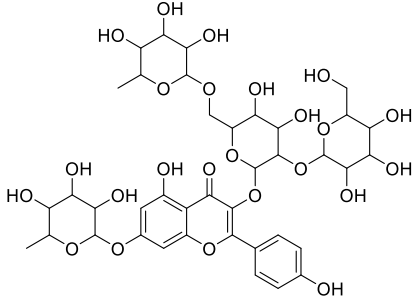
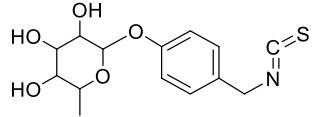
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| 7   | 6-Octadecenoic acid     |    | 282.2558<br>8  | $C_{18}H_{34}O_2$     | [7]  |
| 8   | Nigellidine             |    | 294.1368<br>28 | $C_{18}H_{18}N_2O_2$  | [8]  |
| 9   | Nigellidine 1-O-Sulfate |    | 374.0936<br>43 | $C_{18}H_{18}N_2O_5S$ | [9]  |
| 10  | Nigellamine C.          |  | 530.2780<br>7  | $C_{32}H_{38}N_2O_5$  | [10] |
| 111 | Nigellamine A4.         |  | 616.3148<br>5  | $C_{36}H_{44}N_2O_7$  | [10] |

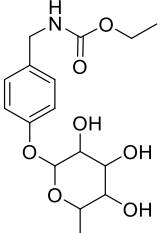
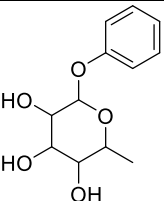
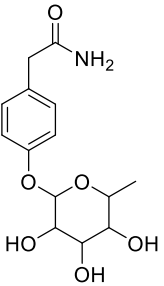
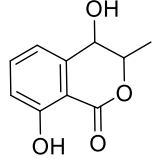
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| 12 | Nigellamine<br>A <sub>3</sub> . |    | 644.3461<br>53 | C <sub>38</sub> H <sub>48</sub> N <sub>2</sub> O <sub>7</sub> | [10] |
| 13 | Nigellamine<br>A <sub>1</sub> . |    | 649.3039<br>54 | C <sub>40</sub> H <sub>43</sub> NO <sub>7</sub>               | [11] |
| 14 | Nigellamine<br>A <sub>5</sub> . |   | 664.3148<br>53 | C <sub>40</sub> H <sub>44</sub> N <sub>2</sub> O <sub>7</sub> | [10] |
| 15 | Nigellamine<br>B <sub>1</sub> . |  | 681.2937<br>84 | C <sub>40</sub> H <sub>43</sub> NO <sub>9</sub>               | [11] |

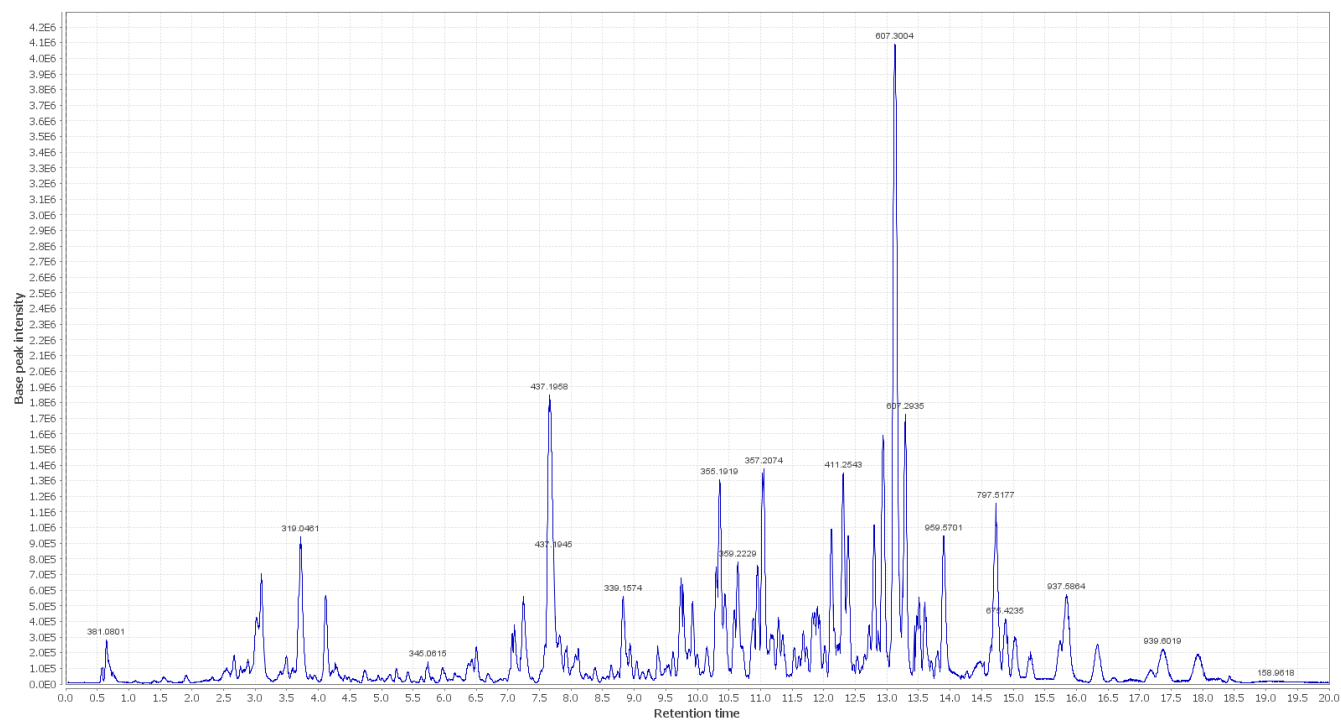
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| 16 | 28-Hydroxy-7-octacosanone.                     |       | 424.428 | C <sub>28</sub> H <sub>56</sub> O <sub>2</sub>  | [12] |
| 17 | Musabalbisiene A                               |    | 498.172 | C <sub>23</sub> H <sub>30</sub> O <sub>12</sub> | [13] |
| 18 | 2-Hydroxyperinaphthene.                        |    | 196.052 | C <sub>13</sub> H <sub>8</sub> O <sub>2</sub>   | [14] |
| 19 | Naproxen.                                      |    | 230.094 | C <sub>14</sub> H <sub>14</sub> O <sub>3</sub>  | [15] |
| 20 | 4-Phenyl-1H,3H-naphtho[1,8-cd]pyran-1,3-dione. |   | 274.062 | C <sub>18</sub> H <sub>10</sub> O <sub>3</sub>  | [14] |
| 21 | 2-Methoxy-9-phenyl-1H-phenalen-1-one.          |  | 286.099 | C <sub>20</sub> H <sub>14</sub> O <sub>2</sub>  | [14] |
| 22 | Musafluorone                                   |  | 300.078 | C <sub>20</sub> H <sub>12</sub> O <sub>3</sub>  | [16] |

|    |                                                      |                                                                                     |                |                                                |      |
|----|------------------------------------------------------|-------------------------------------------------------------------------------------|----------------|------------------------------------------------|------|
| 23 | 9-(4-Hydroxyphenyl)-2-methoxy-1H-phenalen-1-one      |    | 302.094        | C <sub>20</sub> H <sub>14</sub> O <sub>3</sub> | [14] |
| 24 | 9-(3,4-Dimethoxyphenyl)-2-methoxy-1H-phenalen-1-one. |    | 346.120        | C <sub>22</sub> H <sub>18</sub> O <sub>4</sub> | [17] |
| 25 | Bisanigorufone                                       |  | 542.151        | C <sub>38</sub> H <sub>22</sub> O <sub>4</sub> | [18] |
| 26 | Anigorootin                                          |  | 574.141<br>64  | C <sub>38</sub> H <sub>22</sub> O <sub>6</sub> | [19] |
| 27 | 4'-Hydroxyanigorootin.                               |  | 590.136<br>555 | C <sub>38</sub> H <sub>22</sub> O <sub>7</sub> | [20] |
| 28 | 4',4''-Dihydroxyanigorootin.                         |  | 606.131<br>47  | C <sub>38</sub> H <sub>22</sub> O <sub>8</sub> | [20] |

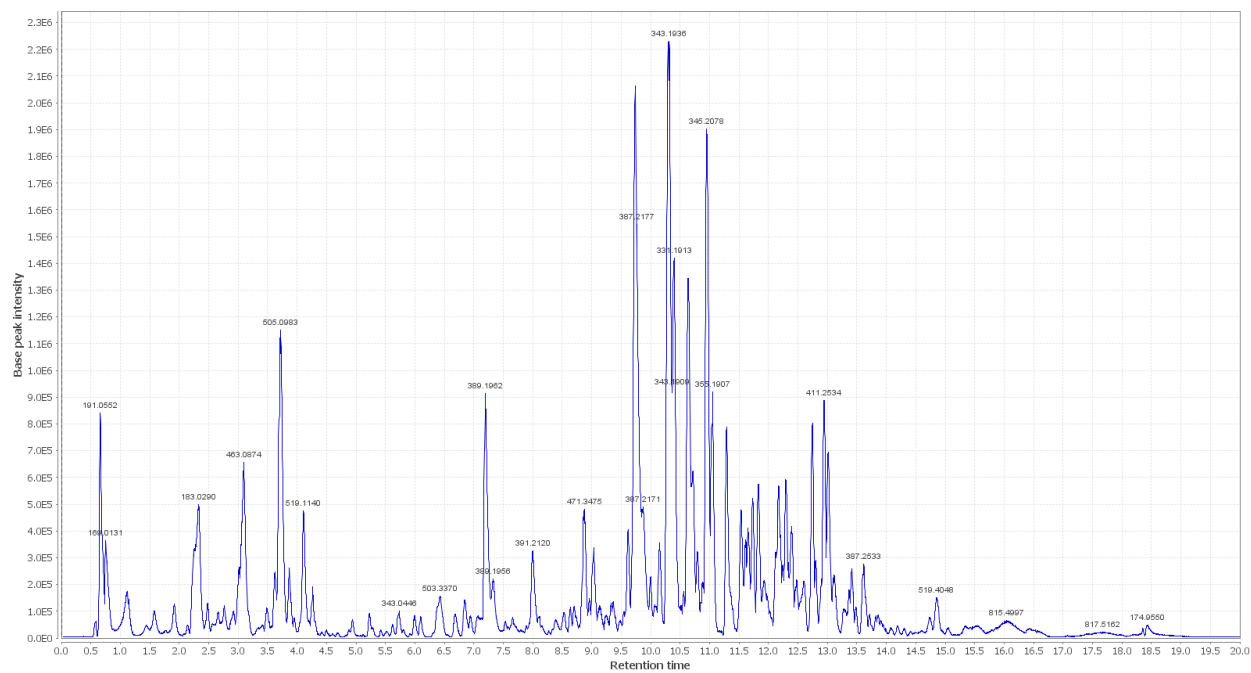
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|----|--------------------------------------------------------------------------|-------------------------------------------------------------------------------------|----------------|----------------------------------------------------------------|------|
| 29 | Mc-FCC-56.<br>Musa cavendish<br>fluorescent<br>chlorophyll<br>catabolite |    | 830.301<br>056 | C <sub>42</sub> H <sub>46</sub> N <sub>4</sub> O <sub>14</sub> | [21] |
| 30 | 24-<br>Methylenepollinasta<br>none                                       |    | 410.354<br>865 | C <sub>29</sub> H <sub>46</sub> O                              | [22] |
| 31 | Moringyne                                                                |   | 312.120<br>90  | C <sub>15</sub> H <sub>20</sub> O <sub>7</sub>                 | [23] |
| 32 | Catechin                                                                 |  | 290.079<br>04  | C <sub>15</sub> H <sub>14</sub> O <sub>6</sub>                 | [24] |
| 33 | Quercetin                                                                |  | 302.042<br>655 | C <sub>15</sub> H <sub>10</sub> O <sub>7</sub>                 | [24] |
| 34 | Kaempferol                                                               |  | 286.047<br>74  | C <sub>15</sub> H <sub>10</sub> O <sub>6</sub>                 | [25] |
| 35 | Gallic acid                                                              |  | 170.021<br>525 | C <sub>7</sub> H <sub>6</sub> O <sub>5</sub>                   | [26] |
| 36 | <i>p</i> -Coumaric acid                                                  |  | 164.047<br>345 | C <sub>9</sub> H <sub>8</sub> O <sub>3</sub>                   | [24] |

|    |                                                                                                                                       |                                                                                     |                |                                                   |      |
|----|---------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|----------------|---------------------------------------------------|------|
| 37 | Ferulic acid                                                                                                                          |    | 194.058        | C <sub>10</sub> H <sub>10</sub> O <sub>4</sub>    | [24] |
| 38 | Caffeic acid                                                                                                                          |    | 180.042<br>26  | C <sub>9</sub> H <sub>8</sub> O <sub>4</sub>      | [24] |
| 39 | Protocatechuic acid                                                                                                                   |    | 154.026<br>61  | C <sub>7</sub> H <sub>6</sub> O <sub>4</sub>      | [24] |
| 40 | Cinnamic acid                                                                                                                         |    | 148.052<br>43  | C <sub>9</sub> H <sub>8</sub> O <sub>2</sub>      | [24] |
| 41 | Ellagic acid                                                                                                                          |    | 302.006<br>27  | C <sub>14</sub> H <sub>6</sub> O <sub>8</sub>     | [25] |
| 42 | Vanillic acid                                                                                                                         |   | 168.042<br>26  | C <sub>8</sub> H <sub>8</sub> O <sub>4</sub>      | [24] |
| 43 | Moringine                                                                                                                             |  | 107.073<br>499 | C <sub>7</sub> H <sub>9</sub> N                   | [27] |
| 44 | Kaempferol 3,7-diglycosides 3-O-[[β-D-Glucopyranosyl-(1→2)-[α-L-rhamnopyranosyl-(1→6)]-β-D-glucopyranoside], 7-O-α-L-rhamnopyranoside |  | 902.269<br>21  | C <sub>39</sub> H <sub>50</sub> O <sub>24</sub>   | [28] |
| 45 | 4-Hydroxybenzyl isothiocyanate O-α-L-rhamnopyranoside                                                                                 |  | 311.082<br>744 | C <sub>14</sub> H <sub>17</sub> NO <sub>5</sub> S | [29] |

|    |                                                                                                         |                                                                                    |                |                                                 |      |
|----|---------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------|----------------|-------------------------------------------------|------|
| 46 | (4-Hydroxybenzyl)<br>carbamic acid ester,<br><i>O</i> - $\alpha$ -L-<br>rhamnopyranoside                |   | 341.147<br>454 | C <sub>16</sub> H <sub>23</sub> NO <sub>7</sub> | [30] |
| 47 | Rhamnose; $\alpha$ -L-<br>Pyranose-form,<br>Phenolic glycoside                                          |   | 240.099<br>7   | C <sub>12</sub> H <sub>16</sub> O <sub>5</sub>  | [31] |
| 48 | 4-<br>Hydroxyphenylacetic<br>acid amide, <i>O</i> - $\alpha$ -<br>L-<br>rhamnopyranoside                |   | 297.121<br>239 | C <sub>14</sub> H <sub>19</sub> NO <sub>6</sub> | [31] |
| 49 | 3,4-Dihydro-4,8-<br>dihydroxy-3-<br>methyl-1H-2-<br>benzopyran-1-one;<br>(3 <i>R</i> ,4 <i>S</i> )-form |  | 194.057<br>91  | C <sub>10</sub> H <sub>10</sub> O <sub>4</sub>  | [32] |

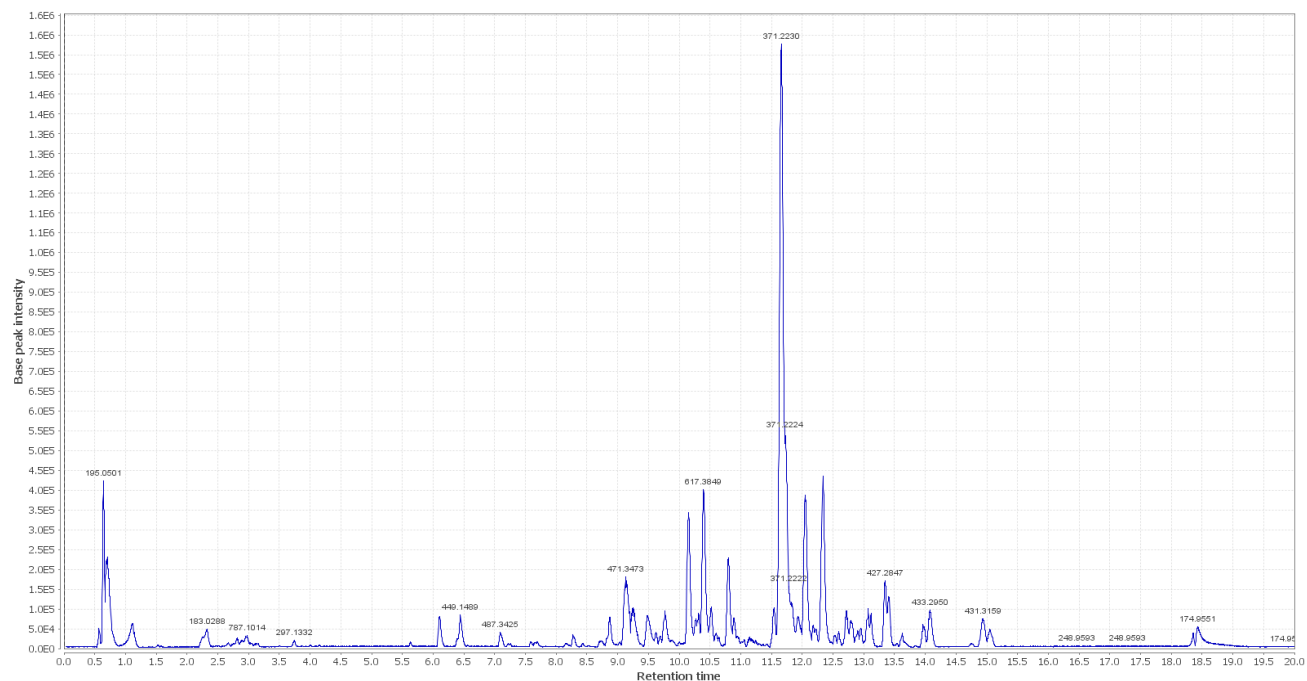


**A**

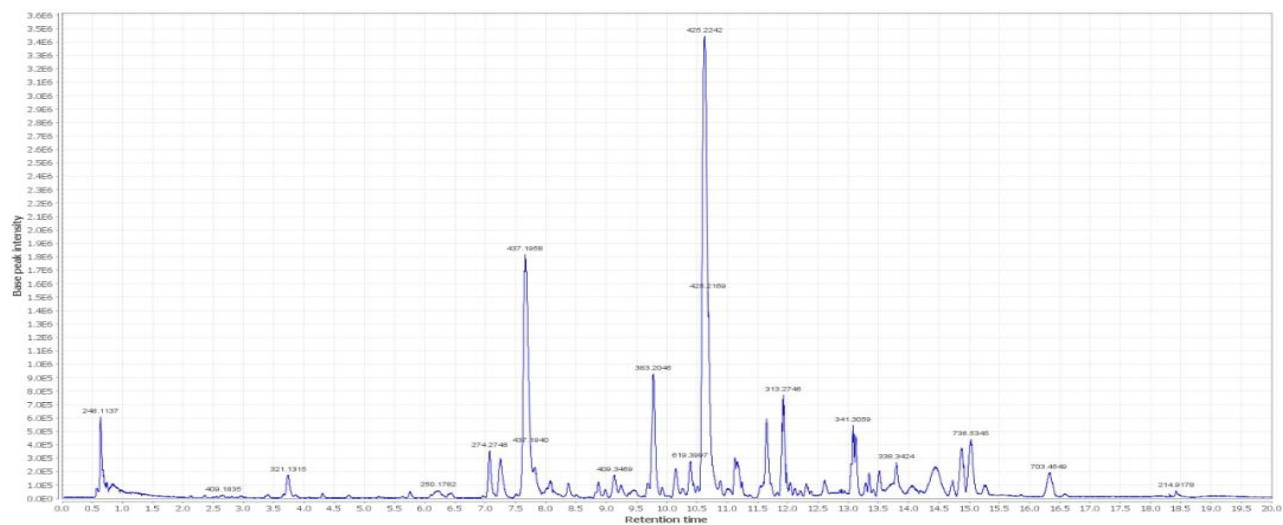


**B**

**Figure S7: Total ion chromatogram of *Nigella Sativa* A ( Positive mode), B (Negative mode).**

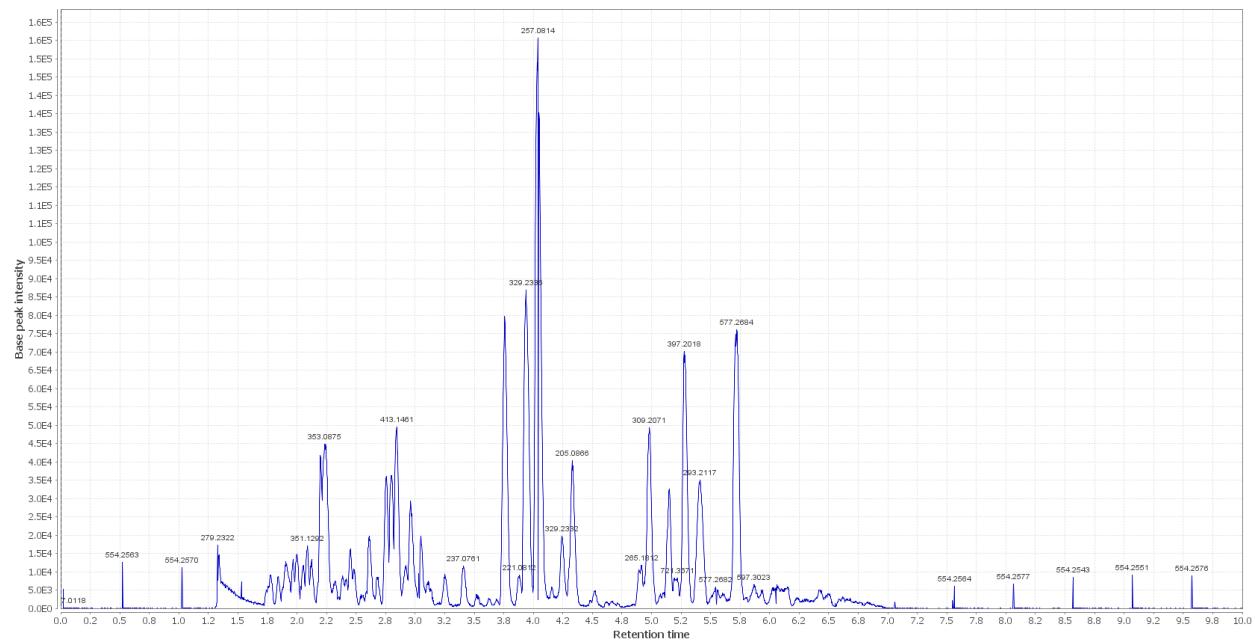


**A**

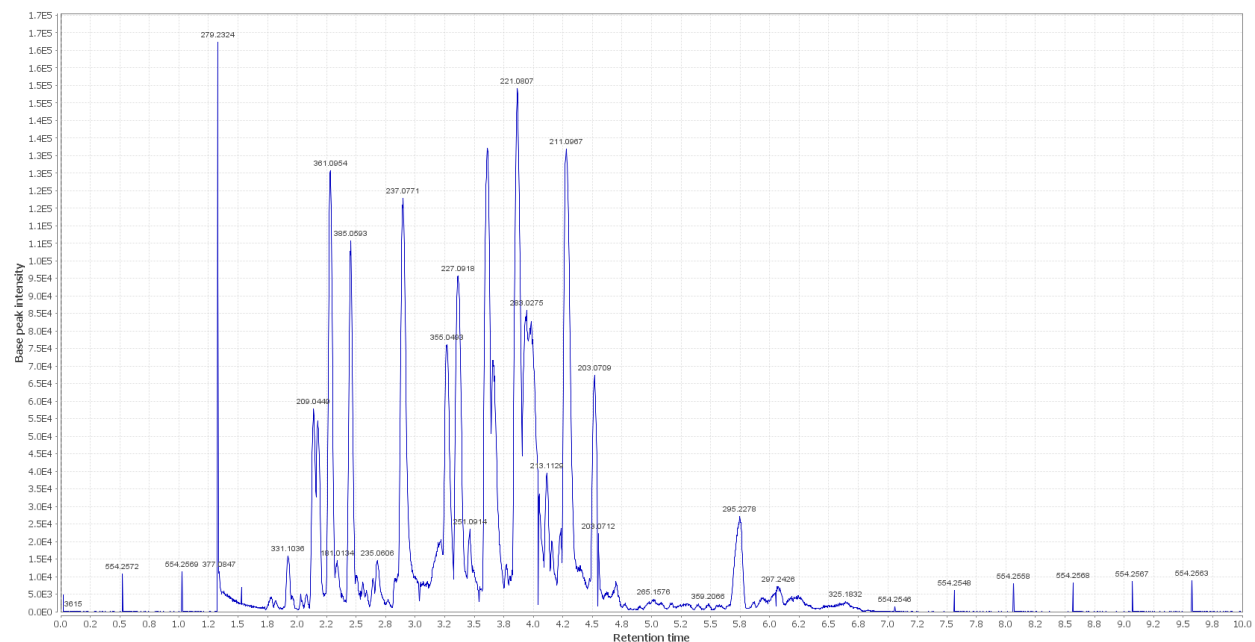


**B**

**Figure S8: Total ion chromatogram of *Musa acuminata* A ( positive mode), B (Negative mode).**



A



B

**Figure S9: Total ion chromatogram of *Moringa Olifera* A ( positive mode), B (Negative mode).**

**Table S2:** The top 30 biological KEGG pathways identified by Genes of plant mixture genes related to Human papilloma virus.

| NO | Pathway                                                                                                               | Fold Enrichment | nGenes | Genes        |
|----|-----------------------------------------------------------------------------------------------------------------------|-----------------|--------|--------------|
| 1  | Positive regulation of mast cell chemotaxis                                                                           | 345.39          | 2      | VEGFA<br>PGF |
| 2  | Pyrimidine deoxyribonucleoside monophosphate biosynthetic process                                                     | 345.39          | 1      | TYMS         |
| 3  | Peptidyl-serine ADP-ribosylation                                                                                      | 345.39          | 1      | PARP1        |
| 4  | Uracil metabolic process                                                                                              | 345.39          | 1      | TYMS         |
| 5  | DNA ADP-ribosylation                                                                                                  | 345.39          | 1      | PARP1        |
| 6  | VEGF-activated platelet-derived growth factor receptor signaling pathway                                              | 345.39          | 1      | VEGFA        |
| 7  | Positive regulation of cell proliferation by VEGF-activated platelet derived growth factor receptor signaling pathway | 345.39          | 1      | VEGFA        |
| 8  | Prostate epithelial cord elongation                                                                                   | 345.39          | 1      | ESR1         |
| 9  | Tertiary branching involved in mammary gland duct morphogenesis                                                       | 345.39          | 1      | PGR          |
| 10 | Cardiac vascular smooth muscle cell development                                                                       | 345.39          | 1      | VEGFA        |
| 11 | Platelet-derived growth factor production                                                                             | 345.39          | 1      | PTGS2        |
| 12 | Regulation of platelet-derived growth factor production                                                               | 345.39          | 1      | PTGS2        |
| 13 | Regulation of G2/M1 transition of meiotic cell cycle                                                                  | 345.39          | 1      | CDC25A       |
| 14 | Positive regulation of G2/M1 transition of meiotic cell cycle                                                         | 345.39          | 1      | CDC25A       |
| 15 | Regulation of RNA interference                                                                                        | 345.39          | 1      | TERT         |
| 16 | Positive regulation of axon guidance                                                                                  | 345.39          | 1      | VEGFA        |
| 17 | Positive regulation of prolactin secretion                                                                            | 345.39          | 1      | EGFR         |
| 18 | Negative regulation of adherens junction organization                                                                 | 345.39          | 1      | VEGFA        |
| 19 | Regulation of single strand break repair                                                                              | 345.39          | 1      | PARP1        |
| 20 | Response to hydrogen sulfide                                                                                          | 345.39          | 1      | NQO1         |

|    |                                                                  |        |   |              |
|----|------------------------------------------------------------------|--------|---|--------------|
| 21 | Negative regulation of blood-brain barrier permeability          | 345.39 | 1 | VEGFA        |
| 22 | Negative regulation of steroid hormone secretion                 | 345.39 | 1 | PTPN11       |
| 23 | Negative regulation of corticosteroid hormone secretion          | 345.39 | 1 | PTPN11       |
| 24 | Negative regulation of glucocorticoid secretion                  | 345.39 | 1 | PTPN11       |
| 25 | Negative regulation of ATP biosynthetic process                  | 345.39 | 1 | PARP1        |
| 26 | Mammary gland branching involved in pregnancy                    | 296.05 | 2 | PGR<br>ESR1  |
| 27 | Regulation of mast cell chemotaxis                               | 259.05 | 2 | VEGFA<br>PGF |
| 28 | DTTP biosynthetic process                                        | 259.05 | 1 | TYMS         |
| 29 | G2/M1 transition of meiotic cell cycle                           | 259.05 | 1 | CDC25A       |
| 30 | Pyrimidine deoxyribonucleoside triphosphate biosynthetic process | 259.05 | 1 | TYMS         |

Table S3: top 30 biological process identified by plant mixture genes related to Human papilloma virus

| NO | Pathway                                                                                                               | Fold Enrichment | nGenes | Genes        |
|----|-----------------------------------------------------------------------------------------------------------------------|-----------------|--------|--------------|
| 1  | Positive regulation of mast cell chemotaxis                                                                           | 345.39          | 2      | VEGFA<br>PGF |
| 2  | Pyrimidine deoxyribonucleoside monophosphate biosynthetic process                                                     | 345.39          | 1      | TYMS         |
| 3  | Peptidyl-serine ADP-ribosylation                                                                                      | 345.39          | 1      | PARP1        |
| 4  | Uracil metabolic process                                                                                              | 345.39          | 1      | TYMS         |
| 5  | DNA ADP-ribosylation                                                                                                  | 345.39          | 1      | PARP1        |
| 6  | VEGF-activated platelet-derived growth factor receptor signaling pathway                                              | 345.39          | 1      | VEGFA        |
| 7  | Positive regulation of cell proliferation by VEGF-activated platelet derived growth factor receptor signaling pathway | 345.39          | 1      | VEGFA        |
| 8  | Prostate epithelial cord elongation                                                                                   | 345.39          | 1      | ESR1         |
| 9  | Tertiary branching involved in mammary gland duct morphogenesis                                                       | 345.39          | 1      | PGR          |
| 10 | Cardiac vascular smooth muscle cell development                                                                       | 345.39          | 1      | VEGFA        |
| 11 | Platelet-derived growth factor production                                                                             | 345.39          | 1      | PTGS2        |
| 12 | Regulation of platelet-derived growth factor production                                                               | 345.39          | 1      | PTGS2        |
| 13 | Regulation of G2/M1 transition of meiotic cell cycle                                                                  | 345.39          | 1      | CDC25A       |
| 14 | Positive regulation of G2/M1 transition of meiotic cell cycle                                                         | 345.39          | 1      | CDC25A       |
| 15 | Regulation of RNA interference                                                                                        | 345.39          | 1      | TERT         |
| 16 | Positive regulation of axon guidance                                                                                  | 345.39          | 1      | VEGFA        |
| 17 | Positive regulation of prolactin secretion                                                                            | 345.39          | 1      | EGFR         |
| 18 | Negative regulation of adherens junction organization                                                                 | 345.39          | 1      | VEGFA        |
| 19 | Regulation of single strand break repair                                                                              | 345.39          | 1      | PARP1        |
| 20 | Response to hydrogen sulfide                                                                                          | 345.39          | 1      | NQO1         |
| 21 | Negative regulation of blood-brain barrier permeability                                                               | 345.39          | 1      | VEGFA        |

|    |                                                                  |        |   |              |
|----|------------------------------------------------------------------|--------|---|--------------|
| 22 | Negative regulation of steroid hormone secretion                 | 345.39 | 1 | PTPN11       |
| 23 | Negative regulation of corticosteroid hormone secretion          | 345.39 | 1 | PTPN11       |
| 24 | Negative regulation of glucocorticoid secretion                  | 345.39 | 1 | PTPN11       |
| 25 | Negative regulation of ATP biosynthetic process                  | 345.39 | 1 | PARP1        |
| 26 | Mammary gland branching involved in pregnancy                    | 296.05 | 2 | PGR<br>ESR1  |
| 27 | Regulation of mast cell chemotaxis                               | 259.05 | 2 | VEGFA<br>PGF |
| 28 | DTTP biosynthetic process                                        | 259.05 | 1 | TYMS         |
| 29 | G2/M1 transition of meiotic cell cycle                           | 259.05 | 1 | CDC25A       |
| 30 | Pyrimidine deoxyribonucleoside triphosphate biosynthetic process | 259.05 | 1 | TYMS         |

Table S4: The top 30 cellular component identified by plant mixture genes related to Human papilloma virus

| NO | Pathway                                            | Fold Enrichment | nGenes | Genes           |
|----|----------------------------------------------------|-----------------|--------|-----------------|
| 1  | RNA-directed RNA polymerase complex                | 345.39          | 1      | TERT            |
| 2  | Cyclin D2-CDK4 complex                             | 345.39          | 1      | CDK4            |
| 3  | Multivesicular body, internal vesicle              | 259.05          | 1      | EGFR            |
| 4  | Alpha-beta T cell receptor complex                 | 207.24          | 1      | PTPN6           |
| 5  | Sorting endosome                                   | 172.70          | 1      | PTPN1           |
| 6  | Mitochondrial crista                               | 129.52          | 1      | PTPN1           |
| 7  | Transcription preinitiation complex                | 103.62          | 1      | ESR1            |
| 8  | NMDA selective glutamate receptor complex          | 94.20           | 1      | PTK2B           |
| 9  | Telomere cap complex                               | 74.01           | 1      | TERT            |
| 10 | Nuclear telomere cap complex                       | 74.01           | 1      | TERT            |
| 11 | Chromosome, telomeric repeat region                | 74.01           | 1      | TERT            |
| 12 | Cytoplasmic side of endoplasmic reticulum membrane | 64.76           | 1      | PTPN1           |
| 13 | T cell receptor complex                            | 60.95           | 1      | PTPN6           |
| 14 | Apical dendrite                                    | 57.57           | 1      | PTK2B           |
| 15 | Telomerase holoenzyme complex                      | 49.34           | 1      | TERT            |
| 16 | Cyclin-dependent protein kinase holoenzyme complex | 47.10           | 2      | CDK4 CDK1       |
| 17 | Transcriptionally active chromatin                 | 43.17           | 1      | ESR1            |
| 18 | Nuclear outer membrane                             | 35.73           | 1      | PTGS2           |
| 19 | Microvillus membrane                               | 34.54           | 1      | CA9             |
| 20 | Tertiary granule lumen                             | 30.93           | 2      | MMP9 PTPN6      |
| 21 | Mediator complex                                   | 23.03           | 1      | CDK4            |
| 22 | Microvillus                                        | 22.28           | 2      | CA2 CA9         |
| 23 | Ionotropic glutamate receptor complex              | 22.05           | 1      | PTK2B           |
| 24 | Nucleoid                                           | 22.05           | 1      | TERT            |
| 25 | Mitochondrial nucleoid                             | 22.05           | 1      | TERT            |
| 26 | Neurotransmitter receptor complex                  | 21.15           | 1      | PTK2B           |
| 27 | Serine/threonine protein kinase complex            | 19.93           | 2      | CDK4 CDK1       |
| 28 | Chromosome, telomeric region                       | 17.37           | 3      | PARP1 TERT CDK1 |
| 29 | Protein kinase complex                             | 17.13           | 2      | CDK4 CDK1       |
| 30 | Plasma membrane raft                               | 16.58           | 2      | PTGS2 PTPN11    |

Table S5: The top 30 molecular functions identified by plant mixture genes related to Human papilloma virus

| NO | nGenes | Fold Enrichment | Pathway                                                            | Genes        |
|----|--------|-----------------|--------------------------------------------------------------------|--------------|
| 1  | 1      | 345.39          | NADPH dehydrogenase (quinone) activity                             | NQO1         |
| 2  | 1      | 345.39          | Estrogen response element binding                                  | ESR1         |
| 3  | 1      | 345.39          | Vascular endothelial growth factor receptor 1 binding              | VEGFA        |
| 4  | 1      | 345.39          | NAD DNA ADP-ribosyltransferase activity                            | PARP1        |
| 5  | 1      | 259.05          | TFIIB-class transcription factor binding                           | ESR1         |
| 6  | 1      | 259.05          | Epidermal growth factor binding                                    | EGFR         |
| 7  | 1      | 259.05          | Receptor-receptor interaction                                      | FGFR1        |
| 8  | 2      | 230.26          | Nitric-oxide synthase regulator activity                           | ESR1 EGFR    |
| 9  | 1      | 207.24          | Superoxide dismutase activity                                      | NQO1         |
| 10 | 1      | 207.24          | Fibroblast growth factor-activated receptor activity               | FGFR1        |
| 11 | 1      | 207.24          | Oxidoreductase activity, acting on superoxide radicals as acceptor | NQO1         |
| 12 | 1      | 207.24          | Estrogen receptor activity                                         | ESR1         |
| 13 | 1      | 207.24          | Neuropilin binding                                                 | VEGFA        |
| 14 | 1      | 172.70          | Telomerase activity                                                | TERT         |
| 15 | 1      | 172.70          | RNA-directed DNA polymerase activity                               | TERT         |
| 16 | 1      | 172.70          | Arylesterase activity                                              | CA2          |
| 17 | 1      | 172.70          | Phosphorylation-dependent protein binding                          | PTPN6        |
| 18 | 2      | 159.41          | RNA polymerase II CTD heptapeptide repeat kinase activity          | CDK4<br>CDK1 |
| 19 | 1      | 148.03          | Cytochrome-b5 reductase activity, acting on NAD(P)H                | NQO1         |
| 20 | 2      | 138.16          | Carbonate dehydratase activity                                     | CA2 CA9      |
| 21 | 2      | 129.52          | Vascular endothelial growth factor receptor binding                | VEGFA<br>PGF |
| 22 | 1      | 129.52          | NMDA glutamate receptor activity                                   | PTK2B        |
| 23 | 1      | 115.13          | Non-membrane spanning protein tyrosine phosphatase activity        | PTPN11       |
| 24 | 1      | 115.13          | D1 dopamine receptor binding                                       | PTPN11       |
| 25 | 2      | 103.62          | Transcription coactivator binding                                  | ESR1 TERT    |

|    |   |        |                                                                      |                 |
|----|---|--------|----------------------------------------------------------------------|-----------------|
| 26 | 1 | 103.62 | Oxidoreductase activity, acting on NAD(P)H, heme protein as acceptor | NQO1            |
| 27 | 1 | 94.20  | Vascular endothelial growth factor receptor 2 binding                | VEGFA           |
| 28 | 1 | 94.20  | Insulin receptor substrate binding                                   | PTPN11          |
| 29 | 2 | 90.10  | Insulin receptor binding                                             | PTPN11<br>PTPN1 |
| 30 | 1 | 86.35  | Sequence-specific mRNA binding                                       | TYMS            |

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