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Research article

# Antioxidant properties of 5 herbal plants based of pharmacophore modelling

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## Abstract

Malaysian medicinal plants are known to exert therapeutic effects.We have evaluated some species namely *Moringa oleifera* (*M. Oleifera*), *Clinacanthus nutans* (*C. Nutans*), *Rhodomyrtus tomentosa* (*R. tomentosa*), *Arctium lappa*(*A. lappa*) and *Sonneratia alba* (*S. alba*) for their antioxidant properties assisted by using pharmacophore modelling approach. Major compounds were displayed from each plantnamely; 3-caffeoylquinic, benzylglucosinolate, kaempferol, leucodelphinidin and quercetin from *M.oleifera*, adenosine, arctigenin, arctiin, and solasoninefrom *A. lappa*, 2-cis-entadamine A, phaeophytin, clinamides B, isovitexin, and vitexinfrom *C .nutans*, 5-hydroxymethylfurfural, alphitolic acid, betulin, methyl gallate, oleanolic acid from *S. alba* and lupeol, rhodomyrtone A, rhodomyrtone B, rhodomyrtone C and rhodomyrtone D from *R. tomentosa*.

**Key words:** Pharmacophore Modelling, Antioxidant properties, *Moringaoleifera, Clinacanthusnutans, Rhodomyrtus tomentosa, Arctium lappa, Sonneratia alba,* and Ligand-Based Pharmacophore.

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## Introduction

Antioxidant refers to compound, which is able to scavenge, cease formation or counteracting the damaging action of oxidants on cells [1]. They act as reducing agent, hydrogen donor, singlet oxygen quencher and metal chelator. Naturally, our body produces free radicals in small amount for particular functions such as modulation of inflammation, killing pathogens, detoxifying toxins and producing signalling molecules [2-3]. Even though the generation of these free radicals is kept in check by the defences and repairs system, the uncontrolled generation of free radical species, particularly of oxygen species and decreased in antioxidant protection within cells cause oxidative stress to healthy body cells [4]. Excess free radicals participate in various chemical reactions subsequently produce more reactive species of oxygen, nitrogen and sulphur which are linked to many chronic diseases like cancers, cardiovascular diseases, neurological disorder, auto-immune deficiency diseases and degenerative disorders associated with aging [5].

Considering the extensive damages arise from oxidative stress on human health, it is

uncommon that antioxidant is one of the interest compounds in the study of plant medicinal value as it provides protection against various oxidative stress-related diseases. In plants, polyphenols such as flavonoids, phenolic acids, stilbenes, coumarins, and lignin are the interest compounds that possess free radical scavenging activity [6]. In this study antioxidant properties are identified based on pharmacophore modelling; the focus is on five plants from South Asia, namely *Moringa oleifera, Clinacanthus nutans, Rhodomyrtus tomentosa, Arctium lappa* and *Sonneratia alba*.

These plants have been well known for centuries as alternative medicine to cure various diseases. Among the prominent uses of *C. nutan s*are as cure for various types of cancers and skin inflammation while *M. Olifera* and *R. Tomentosa* as anti-diabetic [7-8]. Meanwhile, *A. lappa*has been studied for is anti-inflammatory which can prevent or treat gout attack and *S. alba*as anti-diabetic [9]. The major compounds found in each plant are as follows respectively: 3-caffeoylquinic, benzylglucosinolate, kaempferol, leucodelphinidin and quercetin (M. *oleifera*), adenosine, arctigenin, arctiin, and solasonine (*A. lappa*), 2-cis-entadamine, phaeophytin, clinamides B, isovitexin, and vitexin (*C.nutans*), 5-hydroxymethylfurfural, alphitolic acid, betulin, methyl gallate, oleanolic acid (*S. alba*) and lupeol, rhodomyrtone A, rhodomyrtone B, rhodomyrtone C and rhodomyrtone D (*R. tomentosa*).

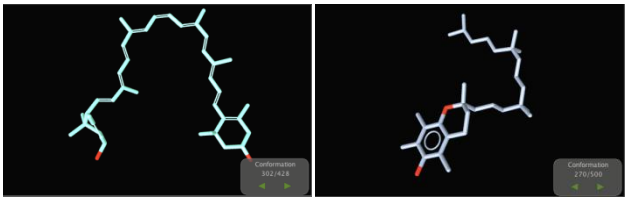
Pharmacophore modelling method simulates the search of potential and promising drugs candidates by virtual screening. Pharmacophore modelling provides useful structural and chemical information for future development of more potent molecules [10].Ligand-based pharmacophore model plays a major role in searching drugs and treatment of certain diseases. Pharmacophore modelling has been applied in combination with other molecular modelling technique [11].

A virtual screening approach was divided into two parts; ligand-based screening and structure-based screening. Ligand-based screening is 2D or 3D chemical structures of known actives molecules of models, which use established selected compounds of interest from a database. The virtual screen was based on the concept of common features and hypothetical geometry of the experimented compounds.

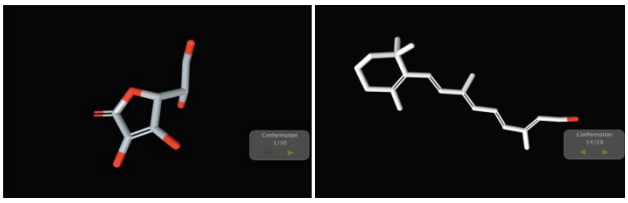
## Materials and methods

### Training Set

A chemical feature-based 3D pharmacophore model was built within the Ligandscout 3.12 OMEGA software. The training set of antioxidant compounds was selected from published data. The selection is essential for generating pharmacophore model. The training set was manipulated for optimization and drawn using ACD/ChemSketch. The optimized training set was listed in Figure 1.



**Lutein** **Retinol**



**Ascorbic Acid** **α-Tocopherol**

**Figure 1. List of training set**

### Hypothesis generation

The ligand-based pharmacophore modelling approach is carried out to evaluate the fit value of compounds isolated from 5 different herbal plants which are *M.oleifera, R.tomentosa. C. nutans, A.lappa*and *S. alba*. A pharmacophore model is generated from selected antioxidant compounds of a set of training sets. The selected test set which consist of components from the 5

herbal plants which are phaeophytin, 2-cis-entadamine A, clinamide B, vetaxin, isovitexin, benzyl glucosinolate, kaempferol, quercentin, leucodelphinidin, betulin, oleanolic acid, aphitolic acid, 5-hydroxymethylfurfural, methyl gallate, arctigenin , solasonine, arctiin , adenosine, lupeol and rhodomyrtone A,B,C and D.

## Results and Discussion

Pharmacophore model generated based on the selected training set (lutein, α-tocopherol, retinol and ascorbic acid) and the features obtained in the pharmacophore modelare shown in Figure 2 and Table 1. Along obtaining the proximity of the training set with the test set (3-caffeoylquinic, benzylglucosinolate, kaempferol, leucodelphinidin, quercetin, adenosine, arctigenin, arctiin, kaempferol, solasonine, 2-cis-entadamine, phaeophytin, clinamides B, isovitexin, vitexin, 5-hydroxymethylfurfural, alphitolic acid, betulin, methyl gallate, oleanolic acid, lupeol, rhodomyrtone A, rhodomyrtone B, rhodomyrtone C and rhodomyrtone D) 10 models of ligand based score fit values are confirmed according to the configuration of each chemical structure respectively as shown in Table 2. 0-1 is the ligand based score fit value range whereby the pharmacophore model closest to 1 is the best model be evaluated. The pharmacophore model feature is evaluated based on model 1. Table 3 shows the fit value and pharmacophore features of training set and test set based on the generated pharmacophore model and Figure 3 (i-xxviii) illustrates the pharmacophore interaction of the test sets and training sets.

**Table 1. Features of the pharmacophore model**

| Features | Interactions |
|---|---|
| | Hydrophobic |
| | Hydrogen Bond Acceptor |
| | Hydrogen Bond Donor |

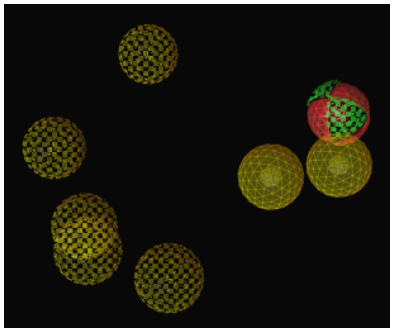


**Figure 2. Pharmacophore model**

**Table 2. Number of models generated and score fit values.**

| Models | Score Fit Value |
|---|---|
| 1 | 0.6559 |
| 2 | 0.2961 |
| 3 | 0.2938 |
| 4 | 0.2902 |
| 5 | 0.2900 |
| 6 | 0.2841 |
| 7 | 0.2754 |
| 8 | 0.2506 |
| 9 | 0.2497 |
| 10 | 0.2451 |

Ligand based drug design is where the chemical structure and pharmacophore features proximity are obtained by aligning the pharmacophore model generated based on selected training set with the test set using Ligand Scout 3.12 Omega Software. There are several pharmacophore features; whereby through generating the pharmacophore model features such as hydrogen bond acceptor (HBA), hydrogen bond donor (HBD) and hydrophobic (Hy) are obtained. From the results obtained for an antioxidant remedy the presence of these chemical features are important.

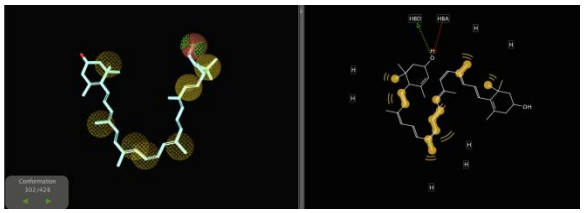
Based on Table 1 and Figure 2, Hy is the main chemical feature represents a compound containing the properties as an antioxidant. The Hy interaction is evaluated by the presence of the methyl functional group in an aromatic structured compound. HBD interaction is obtained due to the presence of the hydroxyl group, sulphate group and imine group whereas for HBA interaction obtained due to the

presence of carbonyl group, hydroxyl group, thioether group and ether group.

Model 1 from the generated pharmacophore based on Table 2 was chosen to be evaluated because the fit value of model 1 is the closest to 1. Through this model, it is found that 6 test sets have better antioxidant property than retinol and ascorbic Acid. Solosonine, betulin, phaeophytin, arctiin, lupeol and arctigenin are in between three training sets which can be observed as having potential antioxidant properties. 14 test sets possess mild antioxidant properties as shown in Table 3 and Figure 3. They are placed in between α-tocopherol and ascorbic acid due to lack of hydrophobic and hydrogen bond acceptor features, which represents the properties of an antioxidant. Further training set and 4 other test sets are not compatible for antioxidant properties due to the structure scaffold and absence of the chemical features.

**Table 3. Fit value and pharmacophore features of training set and test set.**

| Name | Type | Pharmacophore Features | Pharmacophore FitValue |
|---|---|---|---|
| Lutein | Training | | 73.6600 |
| α-Tocopherol | Training | | 62.5400 |
| Solasonine | Test | | 58.7900 |
| Betulin | Test | | 56.6100 |
| Phaeophytin | Test | | 48.4900 |
| Arctiin | Test | | 46.8200 |
| Lupeol | Test | | 45.4900 |
| Arctigenin | Test | | 44.4400 |
| Retinol | Training | | 42.8400 |
| Rhodomyrtosone B | Test | | 42.7200 |
| Oleanolic Acid | Test | | 42.3600 |
| Aphitolic Acid | Test | | 42.3500 |
| Rhodomyrtosone A | Test | | 36.7200 |
| Quercetin | Test | | 35.4700 |
| 3- caffeoylquinic | Test | | 35.4700 |
| Rhodomyrtosone C | Test | | 35.4600 |
| 2-cis- Entadamide | Test | | 35.4600 |
| Benzylglucosinolate | Test | | 35.4500 |
| Vitexin | Test | | 35.4400 |
| Kaempferol | Test | | 35.3300 |
| Isovetaxin | Test | | 35.3300 |
| 5-hydroxyxethylfuran | Test | | 34.9900 |
| Clinamide B | Test | | 33.0200 |
| Ascorbic Acid | Training | | 0.0000 |
| Methyl Gallate | Test | | 0.0000 |
| Rhodomyrtosone D | Test | | 0.0000 |
| Leucodelphinidin | Test | | 0.0000 |
| Adenosine | Test | | 0.0000 |



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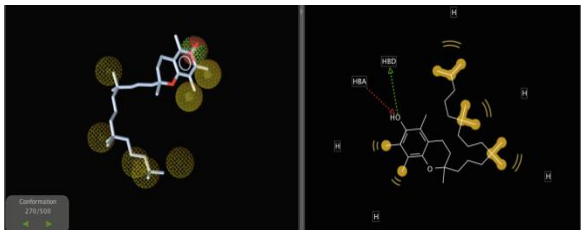

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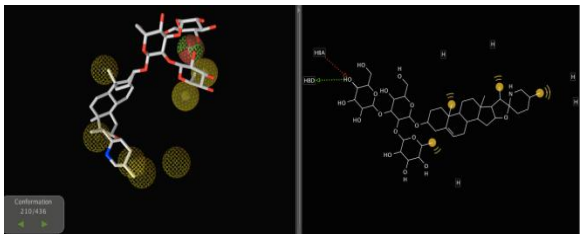

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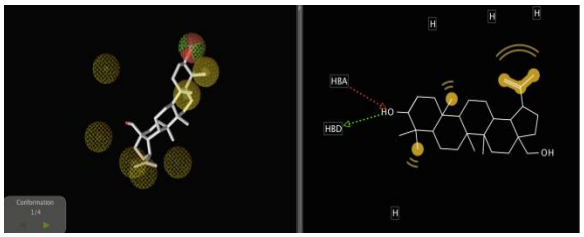

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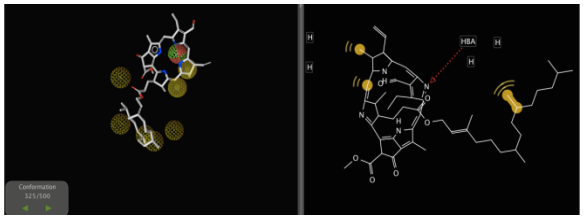

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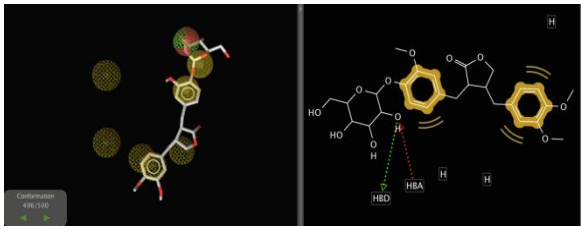

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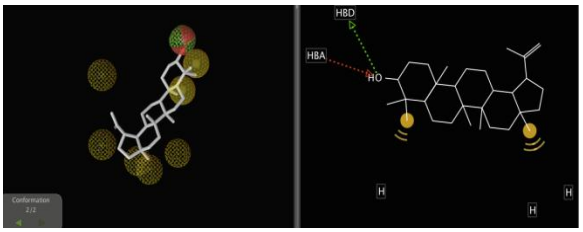

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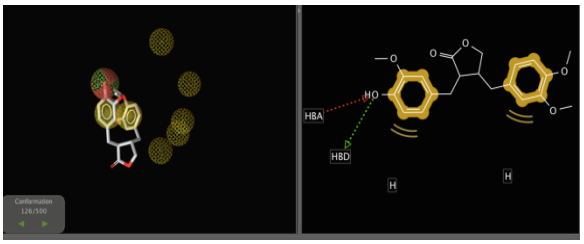

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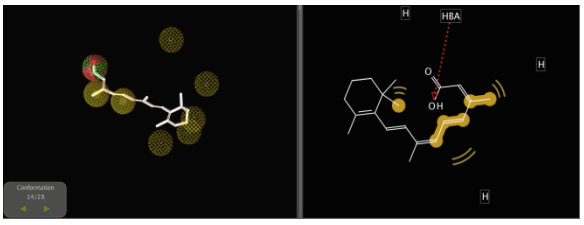

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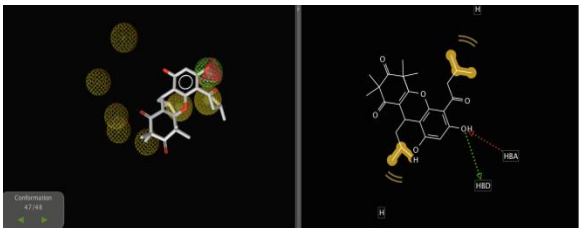

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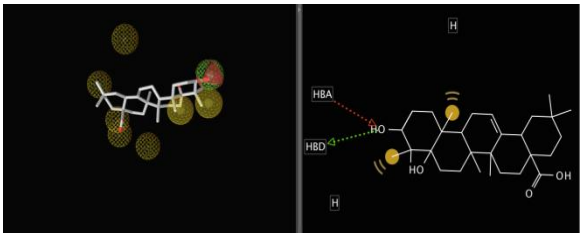

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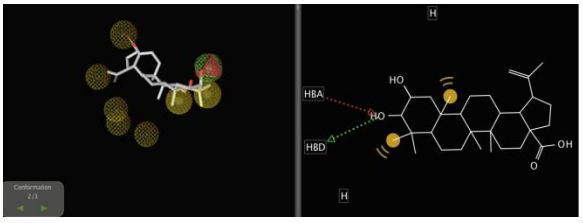

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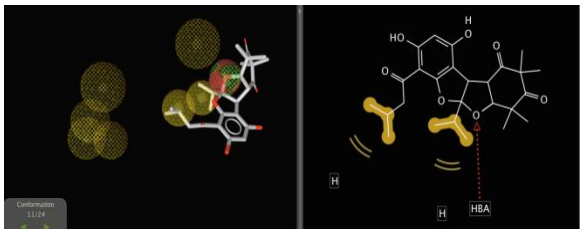


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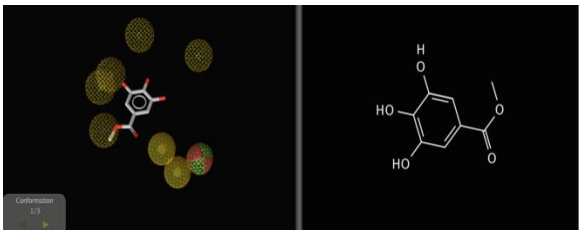

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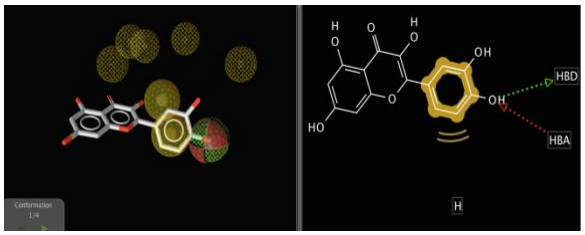


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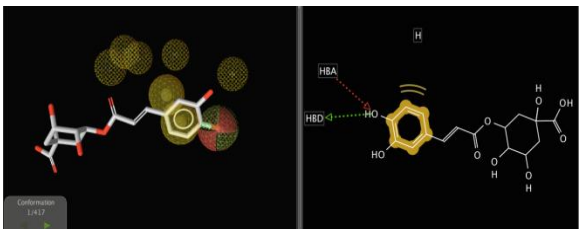


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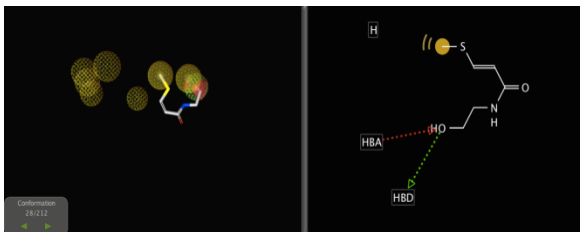


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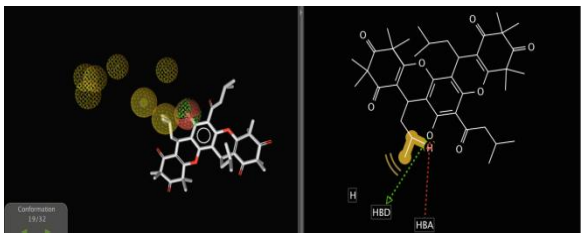


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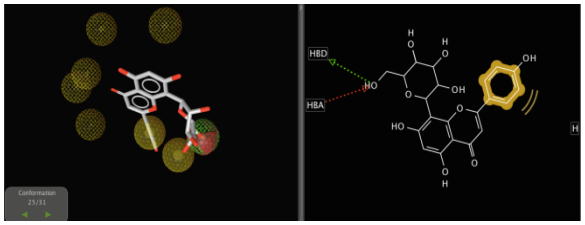


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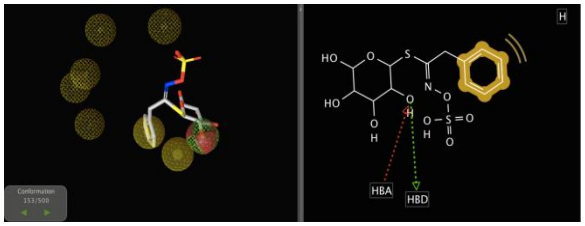


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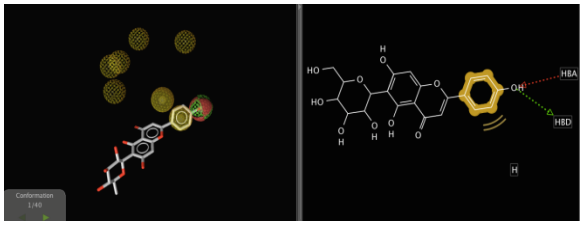


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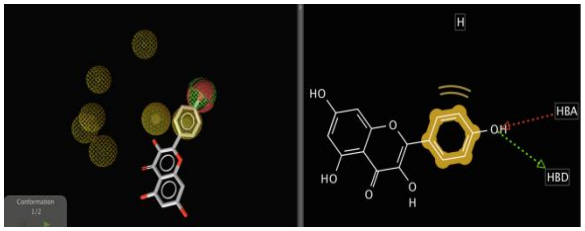


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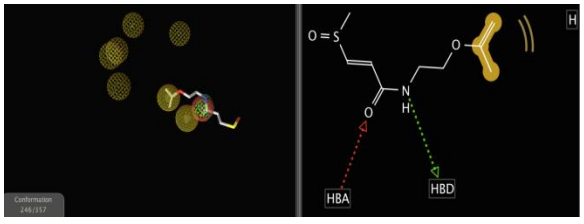


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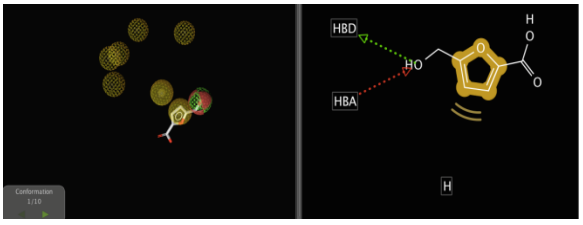


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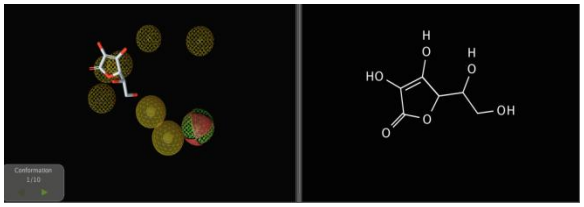

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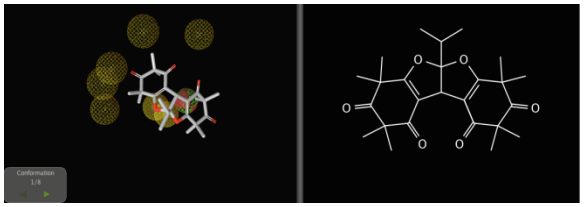

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**Figure 3. Pharmacophore interaction of pharmacophore model and test set**

## Conclusion

In conclusion, the presence of hydrophobic, hydrogen bond donor and hydrogen bond acceptor are the necessary chemical features for antioxidant properties. Based on the results obtained solasonine, arctiin and arctigenin from *A. lappa*, belutin from *S.alba* and lupeol from *R.tomentosa* possess the properties of antioxidant. The other 14 chemical constituents possess mild antioxidant properties which can be enhanced through combining compounds that possess the features of hydrophobic.

## Acknowledgment

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