CODEN IEJMAT *Internet Electronic Journal of Molecular Design* **2005**, *4*, 803–812 ISSN 1538–6414
BioChem Press http://www.biochempress.com

Inter*net* Electronic Journal of Molecular Design

November 2005, Volume 4, Number 11, Pages 803–812

Editor: Ovidiu Ivanciuc

Special issue dedicated to Professor Danail Bonchev on the occasion of the 65th birthday

# Structure–Antifungal Activity Relationships of Some Organic Compounds with Varying Number of Hydroxyl Groups for their Inhibition of *Colletotrichum gloeosporioides*

Eugene Sebastian J. Nidiry

Indian Institute of Horticultural Research, Hessaraghatta Lake P. O., Bangalore 560089, India

Received: January 9, 2004; Revised: June 19, 2005; Accepted: June 21, 2005; Published: November 30, 2005

**Citation of the article:**
E. S. J. Nidiry, Structure–Antifungal Activity Relationships of Some Organic Compounds with Varying Number of Hydroxyl Groups for their Inhibition of *Colletotrichum gloeosporioides*, *Internet Electron. J. Mol. Des.* **2005**, *4*, 803–812, http://www.biochempress.com.

**Inter*net* Electronic Journal of Molecular Design**

**BioChem Press**
http://www.biochempress.com

# Structure–Antifungal Activity Relationships of Some Organic Compounds with Varying Number of Hydroxyl Groups for their Inhibition of *Colletotrichum gloeosporioides* #

Eugene Sebastian J. Nidiry *

Indian Institute of Horticultural Research, Hessaraghatta Lake P. O., Bangalore 560089, India

Received: January 9, 2004; Revised: June 19, 2005; Accepted: June 21, 2005; Published: November 30, 2005

*Internet Electron. J. Mol. Des*. **2005**, *4* (11), 803–812

**Abstract**

**Motivation.** Hydroxyl group(s) is (are) present in some compounds, which are antifungal as well as in some which promote fungal growth. It was thought interesting to study the structure–antifungal activity relationships of some common alcohols, phenols and carboxylic acids with varying number of hydroxyl groups.

**Method.** Poisoned food technique was used in the determination of percent mycelial growth inhibition of *Colletotrichum gloeosporioides* by the compounds on potato–dextrose–agar medium and probit analysis was used for the computation of median effective concentrations. Evaluation of ClogP values for all compounds was done using Rekker fragment constants. Multiple regression analysis was used in the QSAR study.

**Results.** The very large variation in median effective concentrations ranging from more than 50000 mg/L [$pEC_{50}$ (moles/L) = 0.19] in the case of glycerol to less than 50 mg/L [$pEC_{50}$ (moles/L) = 3.50] in the case of 2–naphthol shows the dramatic effect of the environment within the molecule on the antifungal activity of compounds with hydroxyl groups. While monohydroxy alcohols in general exhibit antifungal activity, the presence of another hydroxyl group has adverse effect on the activity. Introduction of hydroxyl group appears to have detrimental effect on the antifungal activity of aliphatic and aromatic carboxylic acids also. However, substantial differences among the antifungal activities of dihydroxy and trihydroxy phenols indicate that the positions of the hydroxyl groups also play their roles in their activities.

**Conclusions.** The reduction in lipophilicity of the molecule on the introduction of additional hydroxyl groups can be attributed as the reason for the detrimental effect on the antifungal activity of alcohols and carboxylic acids. In the case of phenols, in addition to reduction in lipophilicity, positions of the hydroxyl groups also play their roles in the determination of antifungal activity.

**Keywords.** Hydroxyl group; antifungal activity; *Colletotrichum gloeosporioides*; structure–activity relationships; alcohols; phenols; carboxylic acids.

**Abbreviations and notations**

| | |
|---|---|
| $EC_{50}$, median effective concentration (mg/L) for the mycelial growth inhibition of *Colletotrichum gloeosporioides* | QSAR, quantitative structure–activity relationships |
| | ClogP, calculated partition coefficient |
| | LogP(exp), experimental partition coefficient |

# Dedicated on the occasion of the 65th birthday to Danail Bonchev.

* Correspondence author; E–mail: nidiry@yahoo.co.in.

# 1 INTRODUCTION

The hydroxyl group is one of the most important functional groups of naturally occurring organic molecules [1]. The extensive use of some alcohols and phenols as disinfectants and the use of some chlorinated alcohols and phenols as fungicides in plant disease management [2] may prompt anybody to the generalization that hydroxyl group imparts antifungal activity to molecules. But it is also noteworthy that hydroxyl group is present in all carbohydrates and some other growth factors which are required for fungal growth [3]. In view of these facts, it was thought interesting to study the effect of additional hydroxyl group(s) on the antifungal activity of some alcohols and phenols and the introduction of hydroxyl group in some carboxylic acids so that it can be guidance for the synthesis of antifungal compounds with or without hydroxyl groups. In the present study, the median effective concentrations of some common alcohols, phenols and carboxylic acids with varying number of hydroxyl groups for the mycelial growth inhibition of *Colletotrichum gloeosporioides* on potato–dextrose–agar medium were computed and compared. Structure–activity relationships (SAR) and quantitative structure–activity relationships (QSAR) of the compounds are discussed.

# 2 MATERIALS AND METHODS

## 2.1 Chemicals

Twenty–one compounds given in Table 1 were tested for antifungal activity. In this set, compounds **1** to **3** are monohydroxy alcohols, compound **4** is a dihydroxy alcohol and compound **5** is a trihydroxy alcohol. Compounds **6**, **12** and **13** are monohydroxy phenols, compounds **7** to **9** are dihydroxy phenols and compounds **10** to **11** are trihydroxy phenols. Compounds **14**, **15** and **17** are monocarboxylic acids, compounds **16** and **18** are monohydroxy monocarboxylic acids, compound **19** is a dicarboxylic acid, compound **20** is a dihydroxy dicarboxylic acid and compound **21** is a monohydroxy tricarboxylic acid. All compounds were obtained commercially.

## 2.2 Biological Activity Data

The percent mycelial growth inhibition of *Colletotrichum gloeosporioides* at five different concentrations of all compounds given in Table 1 was determined by poisoned food technique [4] detailed in an earlier paper [5]. All compounds were soluble either in water or acetone. Appropriate amounts of the compounds dissolved in either distilled water or acetone (0.25 ml) were added to 30 ml of sterilized media to get the required concentrations, the same quantity of acetone being added in the control and in the cases of water soluble compounds also. Maintenance of acetone free controls revealed that this concentration of acetone did not inhibit the mycelial growth of the fungus. Mycelial discs of *C. gloeosporioides* were aseptically transferred to the center of Petri

plates and the Petri dishes were incubated at 27±2°C for 5 days. The percent mycelial growth inhibition (P) at each concentration with respect to the control, after giving due adjustment to the initial diameter (0.8 cm) of the mycelial disc, was calculated by the formula,

$$P = 100\frac{C - T}{T}$$

where T is the diameter of the mycelial growth of the treated one and C that of the control. Each treatment was replicated twice and the averages of the values were obtained. These percentages were converted to probits and median effective concentrations, $EC_{50}$ (mg/L), of the compounds were computed by probit analysis [6]. These values were converted to $pEC_{50}$ (moles/L), which is equal to the negative logarithm of median effective molar concentration for QSAR studies.

## 2.3 Partition Coefficients

Experimentally determined octanol–water partition coefficients (LogP) of many compounds given in Table 1 are available in literature [7]. There are differences in the LogP values determined by different workers. For four compounds, namely, glycerol, pyrogallol, oxalic acid and tartaric acid, these values have not been reported. Moreover, if one gives importance to the predictive values of the equations to be developed in QSAR study, it is better to take calculated partition coefficients (ClogP). In view of these facts, ClogP values were evaluated for all the compounds using Rekker fragment constants by the method described by Hansch and Leo [7]. The fragment constants used were: $f_H = 0.23$; $fc_{(aliphatic)} = 0.20$; $fc_{(aromatic)} = 0.13$ ; $f_{CH(aromatic)} = 0.35$; $f_{C(aromatic\ ring\ fusion)} = 0.22$; $f_{phenyl} = 1.90$; $f_{OH(aliphatic)} = –1.64$; $f_{OH(aromatic)} = –0.44$; $f_{COOH(aliphatic)} = –1.11$; $f_{COOH(aromatic)} = –0.42$; and $f_{C–C\ bond} = –0.12$ (n–1), where 'n' is the number of C–C bonds. The calculated partition coefficients (ClogP) values of all the twenty–one compounds are presented in Table 1.

In order to test the reliability of this method of calculation, a correlation study of the experimentally determined LogP values of seventeen compounds reported in literature [7] (presented in Table 1) and their ClogP values was done. The significant correlation ($r$ = 0.954, significant at 0.01 level) revealed that the method of computation of ClogP values is reliable.

## 2.4 Multiple Regression

This was done by the software OpenStat 2, Version 5.2.1 available on the Internet [8].

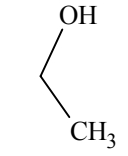
# 3 RESULTS AND DISCUSSION

In Table 1 we present median effective concentrations [$EC_{50}$ (mg/L)] along with negative logarithms median effective molar concentrations [$pEC_{50}$ (moles/L)] for the mycelial growth inhibition of *Colletotrichum gloeosporioides* of all the twenty–one compounds. The very large

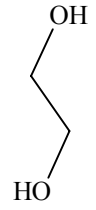
variation in the median effective concentrations ranging from more than 50000 mg/L in the case of glycerol to less than 50 mg/L in the case of 2–naphthol shows the dramatic role of environment within the molecule on the antifungal activity of organic compounds with hydroxyl group(s).

**Table 1.** Antifungal activity of some alcohols, phenols, carboxylic acids and hydroxy carboxylic acids ($EC_{50}$ = median effective concentration for mycelial growth inhibition in mg/L; $pEC_{50}$ = negative logarithm of median effective molar concentration for mycelial growth inhibition) with partition coefficients [LogP(exp) = experimentally determined reported partition coefficients; ClogP = calculated partition coefficients; NR = not reported].

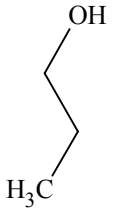
| No | Compound | $EC_{50}$ | $pEC_{50}$ | LogP(exp) | ClogP |
|---|---|---|---|---|---|
| **1** | Methanol | 24687 | 0.11 | –0.77 | –0.75 |
| **2** | Ethanol | 17683 | 0.42 | 0.10 | –0.09 |
| **3** | Propanol | 8979 | 0.83 | 0.25 | 0.45 |
| **4** | Ethylene glycol | 34050 | 0.26 | –1.93 | –1.96 |
| **5** | Glycerol | 59665 | 0.19 | NR | –3.17 |
| **6** | Phenol | 233 | 2.61 | 1.48 | 1.46 |
| **7** | Catechol | 239 | 2.66 | 1.01 | 0.79 |
| **8** | Resorcinol | 1540 | 1.85 | 0.77 | 0.79 |
| **9** | Hydroquinone | 1716 | 1.81 | 0.50 | 0.79 |
| **10** | Pyrogallol | 458 | 2.44 | NR | 0.12 |
| **11** | Phloroglucinol | 9959 | 1.10 | 0.16 | 0.12 |
| **12** | 1–Naphthol | 60 | 3.38 | 2.98 | 2.58 |
| **13** | 2–Naphthol | 46 | 3.50 | 2.84 | 2.58 |
| **14** | Acetic acid | 838 | 1.85 | –0.17 | –0.22 |
| **15** | Propionic acid | 343 | 2.33 | 0.33 | 0.44 |
| **16** | Lactic acid | 4767 | 1.28 | –0.62 | –1.43 |
| **17** | Benzoic acid | 843 | 2.16 | 1.87 | 1.87 |
| **18** | 4–Hydroxy benzoic acid | 2485 | 1.75 | 1.58 | 1.20 |
| **19** | Oxalic acid | 1153 | 1.89 | NR | –2.22 |
| **20** | Tartaric acid | 5230 | 1.46 | NR | –4.64 |
| **21** | Citric acid | 6703 | 1.46 | –1.72 | –3.57 |



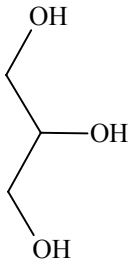

**2**
$pEC_{50}$ = 0.42




**4**
$pEC_{50}$ = 0.26




**3**
$pEC_{50}$ = 0.83




**5**
$pEC_{50}$ = 0.19

**Figure 1.** Antifungal activities of some alcohols with varying number of hydroxyl groups.

## 3.1 Alcohols

The first five compounds in Table 1 are alcohols, consisting of three monohydroxy, one dihydroxy and one trihydroxy alcohol. It is very clear that the presence of additional hydroxyl group has dramatic adverse effect on the activity of alcohols. The structures of the C2 monohydroxy alcohol, C2 dihydroxy alcohol, C3 monohydroxy alcohol and C3 trihydroxy alcohol along with their activities are given in Figure 1 for comparison.

The earlier QSAR studies on monohydroxy alcohols had revealed that their antifungal activity is mainly dependent on hydrophobicity of the alkyl moiety [9,10,11]. However, the effect of additional hydroxyl groups on the antifungal activity was not studied quantitatively. A QSAR study on the first five compounds in Table 1, which are all alcohols, was attempted. The following relationship was found between $pEC_{50}$ and calculated partition coefficients.

$$\begin{gathered} pEC_{50} = 0.509(\pm 0.276) + 0.133(\pm 0.161)\ ClogP \\ n = 5 \quad R = 0.682 \quad s = 0.241 \quad F = 2.61 \quad r^2_{LOO} = -0.618 \end{gathered} \tag{1}$$

In this and the following equations, $n$ = number of compounds under study, $R$ = correlation coefficient, $s$ = standard deviation, $F$ = Fisher statistics and $r^2_{LOO}$ = cross–validated squared correlation coefficient obtained for leave–one–out cross–validation. The figures in parenthesis are for 95% confidence interval.

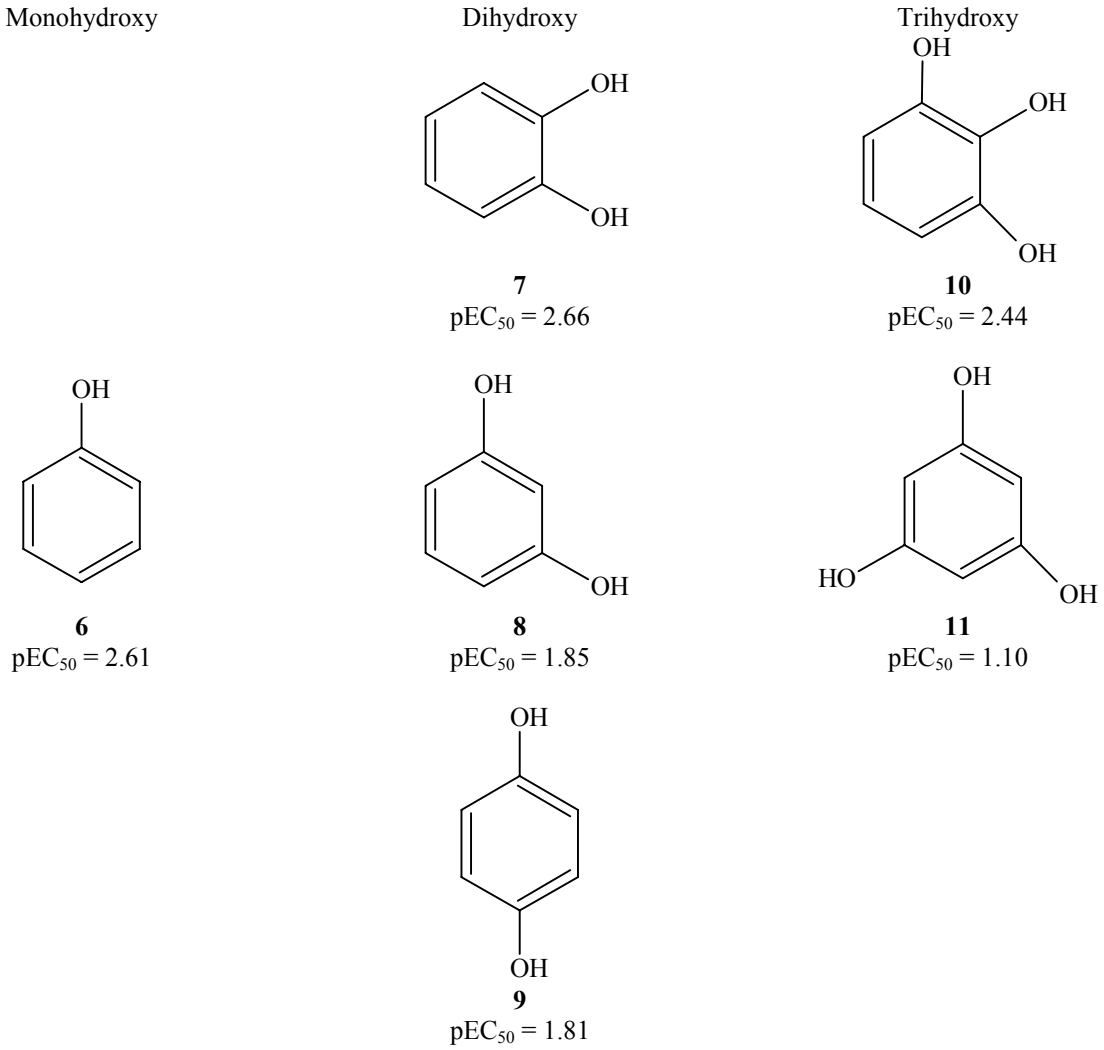
Substitution of ClogP with the parameter $N_{OH}$, depicting the number of hydroxyl groups gave Eq. (2).

$$\begin{gathered} pEC_{50} = 0.585(\pm 0.580) - 0.139(\pm 0.325)\ N_{OH} \\ n = 5 \quad R = 0.437 \quad s = 0.297 \quad F = 0.71 \quad r^2_{LOO} = -0.751 \end{gathered} \tag{2}$$

There is a significant negative correlation between ClogP and $N_{OH}$ ($r$ = –0.96) for the set of five compounds. The $F$ values of Eqs. (1) and (2) show that the equations are not statistically significant and negative values of $r^2_{LOO}$ indicate that they do not have much predictive values.

## 3.2 Phenols

In Table 1, compound **6** is simple phenol, while compounds **7** to **11** are polyhydroxy phenols in which the hydroxyl groups are situated at different positions of the phenyl ring. It can be seen that introduction of another hydroxyl group has in general adverse effect on the activity. However, catechol exhibits higher activity than the other two dihydroxy phenols, namely, resorcinol and hydroquinone. Between the two trihydroxy phenols, pyrogallol and phloroglucinol, the former shows much higher activity than the latter. These observations show that positions of the hydroxyl groups play important roles in determining the activity of dihydroxy and trihydroxy phenols. The structures of the monohydroxy, dihydroxy and trihydroxy phenols and their activities are given in Figure 2 for comparison.




**6**
$pEC_{50}$ = 2.61

**7**
$pEC_{50}$ = 2.66

**8**
$pEC_{50}$ = 1.85

**9**
$pEC_{50}$ = 1.81

**10**
$pEC_{50}$ = 2.44

**11**
$pEC_{50}$ = 1.10

**Figure 2.** Antifungal activities of phenols with varying number and positions of hydroxyl groups.

A QSAR study of the phenols (**6–11** in Table 1) using Free Wilson analysis [12] was carried out. In this analysis, phenol was taken as the reference compound and indicator variables were given for additional hydroxyl groups at *ortho*, *meta* and *para* positions (Table 2). From the initial analysis, it was found that the effects of *ortho* and *meta* hydroxyl groups were more or less similar. Subsequently, only one variable, namely, [*m*,*p*–OH] depicting the number of additional hydroxyl groups on the *meta* and *para* substituents was taken. It may be noted that pyrogallol can be considered as di(*ortho*–hydroxy)phenol or *ortho*–hydroxy *meta*–hydroxy phenol. The analysis was done by both considerations. Since better correlation was obtained by considering it as di (*ortho*–hydroxy) phenol, details of the other analysis are not given here. Nevertheless, it is interesting to note that in the case of antifungal activity, pyrogallol acts as di (*ortho*–hydroxy) phenol rather than *ortho*–hydroxy *meta*–hydroxy phenol.

The following regression equation was obtained when Free Wilson analysis for the antifungal

activity of phenols was done.

$$pEC_{50} = 2.569(\pm0.088) - 0.736(\pm0.088)\ [m,p\text{–OH}]$$
$$n = 6 \quad R = 0.992 \quad s = 0.082 \quad F = 263.31 \quad r^2_{LOO} = 0.932 \tag{3}$$

Introduction of [*o*–OH] depicting the number of hydroxyl groups at the *ortho* position did not significantly improve the correlation. Experimental and calculated values using Eq. (3) are given in Table 2.

**Table 2.** Physicochemical parameters of phenols ($N_{OH}$ = total number of hydroxyl groups; ClogP = calculated partition coefficient; NA = not applicable) along with antifungal activity data [$pEC_{50}$ (E) = experimentally determined activity; $pEC_{50}$(3) = activity calculated by Eq. (3); $pEC_{50}$(6) = activity calculated by Eq. (6); NC = not calculated]

| No | Compounds | Parameters for Free Wilson Analysis | | | | | ClogP | $N_{OH}$ | $pEC_{50}$(E) | $pEC_{50}$(3) | $pEC_{50}$(6) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | [*o*–OH] | [*m*–OH] | [*p*–OH] | [*m*,*p*–OH] | [OH] | | | | | |
| **6** | Phenol | 0 | 0 | 0 | 0 | 0 | 1.46 | 1 | 2.61 | 2.57 | 2.60 |
| **7** | Catechol | 1 | 0 | 0 | 0 | 1 | 0.79 | 2 | 2.66 | 2.57 | NC |
| **8** | Resorcinol | 0 | 1 | 0 | 1 | 1 | 0.79 | 2 | 1.85 | 1.83 | 1.84 |
| **9** | Hydroquinone | 0 | 0 | 1 | 1 | 1 | 0.79 | 2 | 1.81 | 1.83 | 1.84 |
| **10** | Pyrogallol | 2 | 0 | 0 | 0 | 2 | 0.12 | 3 | 2.44 | 2.57 | NC |
| **11** | Phloroglucinol | 0 | 2 | 0 | 2 | 2 | 0.12 | 3 | 1.10 | 1.10 | 1.09 |
| **12** | 1–Naphthol | NA | NA | NA | NA | NA | 2.58 | 1 | 3.38 | NC | 3.44 |
| **13** | 2–Naphthol | NA | NA | NA | NA | NA | 2.58 | 1 | 3.50 | NC | 3.44 |

Compounds **12** and **13** in Table 1 are naphthols, which show substantially higher activity than the other phenols. The higher activity of naphthols must be due to the higher lipophilicity of the molecules since it is already known that the antifungal activity of monohydroxy phenols is mostly governed by lipophilicity considerations [9]. When the phenols including the naphthols were taken for QSAR study, the following regression equations were obtained.

$$pEC_{50} = 1.617(\pm0.537) + 0.695(\pm0.365)\ ClogP$$
$$n = 8 \quad R = 0.837 \quad s = 0.481 \quad F = 13.98 \quad r^2_{LOO} = 0.471 \tag{4}$$

The use of $N_{OH}$, representing the number of hydroxyl groups, did not significantly improve the correlation.

When the data on catechol and pyrogallol were removed, there was dramatic improvement in the correlation as shown in Eqs. (5) and (6).

$$pEC_{50} = 1.081(\pm0.161) + 0.933(\pm0.096)\ ClogP$$
$$n = 6 \quad R = 0.986 \quad s = 0.111 \quad F = 364.61 \quad r^2_{LOO} = 0.976 \tag{5}$$

$$pEC_{50} = 1.750(\pm0.357) + 0.752(\pm0.106)\ ClogP - 0.251(\pm0.131)\ N_{OH}$$
$$n = 6 \quad R = 0.999 \quad s = 0.053 \quad F = 790.04 \quad r^2_{LOO} = 0.992 \tag{6}$$

Experimental and calculated values by Eq. (6) are given in Table 2. Apart from the high correlation obtained, it may be noted that Eq. (6) explains the very large variation in the antifungal activity ranging from 46 mg/L [$pEC_{50}$ (moles/L) = 3.50] in the case of 2–naphthol to 9959 mg/L [$pEC_{50}$ (moles/L) = 1.10] in the case of phloroglucinol. The results clearly show that for phenols with the exception of those having two hydroxyl groups at adjacent (*ortho*) positions, antifungal

activity is determined by hydrophobicity of the aromatic moiety and the number of hydroxyl groups at the *meta* and *para* positions.

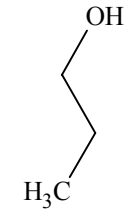
Survey of literature shows several studies on the QSAR of phenols for their antifungal activity [9,13,14,15,16,17] and other antimicrobial activities [18,19]. However, the influence of additional hydroxyl groups and their positions were not manifested in the earlier studies because many phenols with substituents other than hydroxyl groups had also been included in those studies.

It may be noted that while [OH] in Free Wilson analysis [Eq. (3)] is the additional number of hydroxyl groups, $N_{OH}$ depicts the total number of hydroxyl groups in Eq. (6).

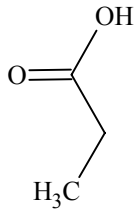
## 3.3 Carboxylic acids

In Table 1, compounds from **14** to **21** are carboxylic acids of which the five compounds from **14** to **18** are monocaboxylic acids. It is clear from the data that the hydroxyl group has detrimental effect on the antifungal activity of monocarboxylic acids. Effect of hydroxyl group on the antifungal activity of aliphatic and aromatic carboxylic acids is shown in Figure 3.

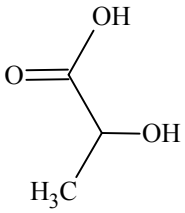
Attempts to understand the quantitative relationship between the antifungal activity and physicochemical parameters of carboxylic acids with and without hydroxyl groups did not give regression equations with significant correlations. One probable reason for this is that apart from the structural features of the compounds the pH of the aqueous medium independently affects the biological activity. It may be noted that the earlier QSAR study on carboxylate ions had revealed the dependence of antifungal activity on lipophilicity of the compounds [9].



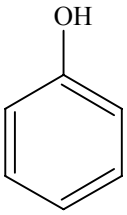

**3**
$pEC_{50}$ = 0.83



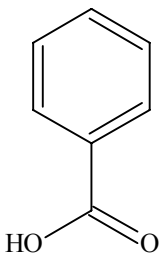

**15**
$pEC_{50}$ = 2.33



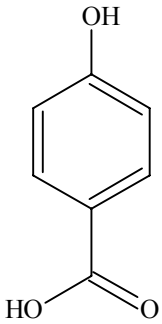

**16**
$pEC_{50}$ = 1.28




**6**
$pEC_{50}$ = 2.61




**17**
$pEC_{50}$ = 2.16




**18**
$pEC_{50}$ = 1.75

**Figure 3.** Antifungal activities of hydroxy compounds, carboxylic acids and hydroxy carboxylic acids.

Hydroxy carboxylic acids can be considered as hydroxy derivatives of carboxylic acids or carboxylic acid derivatives of phenols or alcohols. It may be noted that lactic acid shows higher activity than ethanol, but shows lower activity than propionic acid. This indicates that the lower activity of lactic acid is due the adverse effect hydroxy group on carboxylic acid and not due to carboxylic acid group on the alcohol. Moreover, near values of antifungal activities of acetic acid and oxalic acid with different ClogP values and the substantial difference in the activities of the oxalic acid and its alcohol counterpart diethyl glycol shows that additional carboxylic acid group does not have the same adverse effect as an additional hydroxyl group.

## 4 CONCLUSIONS

The study shows the dramatic adverse effect of additional hydroxyl groups on the antifungal activity of alcohols and phenols and also on the introduction of hydroxyl groups on the activity of aliphatic and aromatic carboxylic acids tested. In the cases of phenols, introduction of additional hydroxyl groups at the adjacent (*ortho*) positions is not found to have adverse effect on the antifungal activity. One probable reason for this anomaly is that the intramolecular hydrogen bonding prevents the intermolecular hydrogen bonding. Although adjacent hydroxyl groups are present in ethylene glycol and glycerol in adjacent carbons, intramolecular hydrogen bonding may not be prevalent because of the free rotation of C–C bonds in these compounds. The planar nature of the phenyl rings and the acidic nature of the phenolic groups together may be favoring the intramolecular hydrogen bonding in catechol and pyrogallol.

It may be noted that the study is based on a limited number of small molecules (C1 to C10) and the conclusions drawn on the adverse effect of additional hydroxyl groups on the antifungal activities of these compounds may not be applicable to large molecules for the lipophilicity considerations mentioned already. Further, the conclusions on the adverse effect of additional hydroxyl groups may not be applicable to compounds containing toxophores other than hydroxyl and carboxylic acid groups as an antifungal polyene ester with as high as ten hydroxyl groups has been reported recently [20].

**Acknowledgment**

The author expresses his gratitude to Director, I. I. H. R. for providing facilities and to Mr. D. N. Mahadevaiah for technical assistance.

## 5 REFERENCES

[1] J. D. Roberts and M. C. Caserio, Basic Principles of Organic Chemistry, W. A. Benjamin, Inc. London, 1977, p. 599.
[2] W. Kramer, Fungicides and bactericides In *Chemistry of Pesticides* (K. H. Buchel, Ed), John Wiley and Sons, New York, 1982, p. 291.
[3] M. O. Garraway and R. C. Evans, *Fungal Nutrition and Physiology*, John Wiley and Sons, 1984, pp. 71–123.

[4] Y. L Nene and P. N Thapliyal, *Fungicides in Plant Disease Control*, Oxford and IBH Publishing Co., New Delhi, 1979, pp. 314–413.
[5] E. S. J. Nidiry, Structure–fungitoxicity relationships of some volatile flavour constituents of the edible mushrooms Agaricus *bisporus* and *Pleurotus florida*, *Flavour Frag. J.* **2001**, *16*, pp. 245–248.
[6] D. J. Finney, *Probit Analysis*, Cambridge University Press, 1981, pp. 283–287.
[7] C. Hansch and A. Leo, *Substituent Constants for Correlation Analysis in Chemistry and Biology*, Wiley, New York, 1979, pp.18–174.
[8] B. Miller, OpenStat 2, Version 5.2.1. http://openstat.homestead.com/OS2.html
[9] C Hansch and E. J. Lien, Structure–activity relationships in antifungal agents, a survey, *J. Med. Chem.* **1971**, *14*, 653–670.
[10] V. K.Gombar and L. Wadhwa, Quantitative structure–activity relationships IV. Use of molecular negentropy as structural parameter, *Arzneim Forsch. /Drug Res*. **1982**, 19, *32* (*II*), 715–718.
[11] E. S. J. Nidiry, Quantitative structure–fungitoxicity relationships of some monohydric alcohols, *J. Agric Food Chem*. **2003**, *51*, 5337–5343.
[12] H. Kubinyi, The quantitative analysis of structure–activity relationships, *Burger's Medicinal Chemistry and Drug Discovery*, Vol I Principles and Practice (Ed, M. E. Wolff) John Wiley and Sons, 1995,p. 520.
[13] M. Polster, B Rittich and R. Zaludova, Relationship between biological activity of phenols and their physico–chemical parameters, *Collection Czechoslovak Chem. Commun*. **1986**, *51*, pp. 241–248.
[14] A. K. Samanta, S. K. Ray, S. C Basak and S. K Bose, Molecular connectivity and antifungal activity. A quantitative structure–activity study of substituted phenols against skin pathogens, *Arzneim– Forsch./Drug Res*. **1982**, *32*, 1515–1517.
[15] K. Voda, B. Boh, and M. Vratacnik, A quantitative structure antifungal activity relationship study of oxygenated aromatic essential oil compounds using data structuring and PLS regression analysis, *Journal of Molecular Modeling* **2004**, *10*, 1, 76–84.
[16] A. Y. Shen, M. I. Tsai, H. Gao and E. J. Lien, Antifungal activities of naphthol derivatives, *Acta Pharm*. **1994**, *44* (2), 109.
[17] K. Voda, B. Boh, M. Vratacnik, F. Pohleven, Effect of antifungal activity of oxygenated aromatic essential oil compounds on the white rot *Trametes versicolor* and the brown rot *Coniphora puterana*, *International Bio deterioration and Biodegradation* **2003**, *51*, 51–59.
[18] S. Shapiro and B. Guggenheim, Inhibition of oral bacteria by phenolic compounds. Part 1. QSAR Analysis using molecular connectivity, *Quant. Struct– Act. Relat*. **1998**, *17*, 4, 327–337.
[19] K. Roy and G. Ghosh, Introduction of Extended Topochemical Atom (ETA) indices in the valence electron mobile (VEM) environment as tools for QSAR/QSPR studies, *Internet Electron. J. Mol. Des*. **2003**, *2*, 599–620.
[20] H. D. Shih, Y.C. Liu, F. L.Hsu, V Mulabagab, R. Dodda and J. W. Huang, Fungichromin, a substance from *Streptomyces padanus* with inhibitory effects on *Rhizoctonia solani*, *J. Agric. Food Chem*. **2003**, *51*, 95–99.

## Biographies

**Eugene Sebastian J. Nidiry** took his M. Sc. from Calicut University, India and did his Ph.D at Indian Agricultural Research Institute, New Delhi, India. He is presently working as Principal Scientist (Organic Chemistry) at Indian Institute of Horticultural Research, Bangalore, India. His areas of special interest are chemical characterization, synthesis and structure–activity relationships of biologically active compounds.