

Contrastive Insillico Study of Natural Acetylcholine Esterase Inhibitors with Chemical Inhibitor

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ABSTRACT

Age related disorders are prominently treated by inhibition of Acetylcholinesterase. 50 million people are believed to be living with Alzheimer or dementia around the world. Currently used drugs for Alzheimer have several neuronal side effects on the elderly. Aged body needs a natural drug with minimal side effects for treatment which will be an effective and natural alternative to its chemical counterparts. Donepezil is the well-known and validated chemical inhibitor which is widely used as a drug for treatment of Alzheimer. Compounds causing delay in the hydrolysis of acetylcholine by Acetylcholinesterase act as a perfect inhibitor. Our study is directed towards virtual screening, high precision docking and molecular dynamics studies to show the stability of natural inhibitors against the already validated chemical inhibitors. 251 natural inhibitors were identified through literature review which were then screened and docked against human recombinant Acetylcholinesterase [1-3]. Glide module of Schrodinger suits were used. Alongside donepezil was also docked against the enzyme. After screening and docking of natural inhibitors compound Diplocone showed the highest gliding score of -11.49. Donepezil showed the gliding score of -8.0. Binding site analysis showed that the interacting amino acids fall into the same binding site map of already validated drug donepezil. Diplocone is then analyzed for 40 nanoseconds through molecular dynamics techniques using Growmac software and found to be stable complex (Diplocone-Ache). Hence, it is convinced that the Diplocone can be a better alternative to its other chemical counterparts.

Keywords: Acetylcholinesterase, Alzheimer, Docking, Natural Inhibitor, Chemical Inhibitor, Molecular Dynamics

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Higher Power Growth of Polynomials with Restricted Zeros

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Abstract:

Let $p(z)$ be a polynomial of degree n having all its zeros on $|z| = k$, $k \leq 1$.

In this paper, we prove a result concerning the higher power growth of $p(z)$ which not only improves as well as generalizes a result proved by Dewan and Ahuja [J. Math. Ineq., 5(3)(2011), 355-361.], but also has interesting implications to earlier results.

Keywords: Polynomial, Polynomial Inequalities, Maximum Modulus.

2010 MSC: 30C10, 30C15.

1. INTRODUCTION

For an arbitrary entire function $f(z)$, we denote $M(f, r) = \max_{|z|=r} |f(z)|$ and higher powers of $M(f, r)$ by $\{M(f, r)\}^s$ where s is a positive integer. It is a simple consequence from maximum modulus principle that [5, Vol. 1, p. 137, Problem III, 269] that for a polynomial $p(z)$ of degree n

$$M(p, R) \leq R^n M(p, 1), \quad R \geq 1. \quad (1.1)$$

The result is best possible and equality occurs in (1.1) for $p(z) = \lambda z^n, \lambda \neq 0$.

If we restrict ourselves to the class of polynomials having no zero in $|z| < 1$, then inequality (1.1) can be sharpened. In fact, it was shown by Ankeny and Rivlin [1] that if $p(z) \neq 0$ in $|z| < 1$, inequality (1.1) can be replaced by

$$M(p, R) \leq \left(\frac{R^n + 1}{2} \right) M(p, 1), \quad R \geq 1. \quad (1.2)$$

Inequality (1.2) is sharp and the extremal polynomial is $p(z) = \alpha + \beta z^n$, where $|\alpha| = |\beta|$.

For the class of polynomials not vanishing in $|z| < k, k \geq 1$, Shah[7] proved that for any $R \geq k$,

$$M(p, R) \leq \left(\frac{R^n + k}{1 + k} \right) M(p, 1) - \left(\frac{R^n - 1}{1 + k} \right) \min_{|z|=k} |p(z)|. \quad (1.3)$$

The result is best possible for $k = 1$ with the polynomial being $p(z) = z^n + 1$.

While trying to obtain inequality analogous to (1.2) for polynomials not vanishing in $|z| < k, k \leq 1$, it had only been able to prove the following result by Dewan and Ahuja [2] for the particular class of polynomials having all its zeros on $|z| = k, k \leq 1$. In fact, they prove

Theorem A. If $p(z) = \sum_{v=0}^n a_v z^v$ is a polynomial of degree n having all its zeros on $|z| = k, k \leq 1$, then for $R \geq 1$ and every positive integer s ,

$$\{M(p, R)\}^s \leq \frac{1}{k^n} \{M(p, 1)\}^s \times \left[\frac{n|a_n| \{k^n(1+k^2) + k^2(R^{ns} - 1)\} + |a_{n-1}|(2k^n + R^{ns} - 1)}{n|a_n|(1+k^2) + 2|a_{n-1}|} \right] \quad (1.4)$$

In this paper, we prove an improvement as well as a generalization of Theorem A which has further interesting implications. More precisely, we obtain

Theorem. If $p(z) = \sum_{v=0}^n a_v z^v$ is a polynomial of degree $n \geq 2$

having all its zeros on $|z|=k, k \leq 1$, then for any arbitrary

complex number $\beta, 1 \leq r \leq R$ and every positive integer s ,

$$\left| \left\{ p(R e^{i\theta}) \right\}^s - \left\{ \beta p(r e^{i\theta}) \right\}^s \right| \leq |1 - \beta^s| \left\{ M(p, r) \right\}^s$$

$$+ A^{s-1} \left[\left\{ M(p, 1) \right\}^s \frac{(R^{ns} - r^{ns})}{k^n} \frac{(n|a_n|k^2 + |a_{n-1}|)}{n|a_n|(1+k^2) + 2|a_{n-1}|} \right.$$

$$\left. - s|a_1| \left(\frac{R^{ns} - r^{ns}}{ns} - \frac{R^{ns-2} - r^{ns-2}}{ns-2} \right) \left\{ M(p, 1) \right\}^{s-1} \right]$$

if $n > 2$ (1.5)

where

$$A = 1 - \left(1 - \frac{1}{r^2} \right) \frac{|a_0|}{M(p, 1)},$$

$$\left| \left\{ p(R e^{i\theta}) \right\}^s - \left\{ \beta p(r e^{i\theta}) \right\}^s \right| \leq |1 - \beta^s| \left\{ M(p, r) \right\}^s$$

$$+ A^{s-1} \left[\left\{ M(p, 1) \right\}^s \frac{R^{2s} - r^{2s}}{k^2} \frac{(2|a_2|k^2 + |a_1|)}{2|a_2|(1+k^2) + 2|a_1|} \right.$$

$$\left. - s|a_1| \left(\frac{R^{2s} - r^{2s}}{2s} - \frac{R^{2s-1} - r^{2s-1}}{2s-1} \right) \left\{ M(p, 1) \right\}^{s-1} \right]$$

if $n = 2$, (1.6)

where

$$A = 1 - \left(1 - \frac{1}{r^2} \right) \frac{|a_0|}{M(p, 1)}.$$

Remark. 1.1. If we put $r=1$ and $\beta=0$ in our theorem and considering maximum, the first two inequalities immediately reduce to a result of Pukhta [6].

Corollary 1.1. If $p(z) = \sum_{v=0}^n a_v z^v$ is a polynomial of degree $n \geq 2$ having all its zeros on $|z|=k, k \leq 1$, then for $R \geq 1$ and

every positive integer s ,

$$\left\{ M(p, R) \right\}^s \leq \left(1 + \frac{R^{ns} - 1}{k^n} \right) \frac{(n|a_n|k^2 + |a_{n-1}|)}{n|a_n|(1+k^2) + 2|a_{n-1}|} \left\{ M(p, 1) \right\}^s$$

$$- s|a_1| \left(\frac{R^{ns} - 1}{ns} - \frac{R^{ns-2} - 1}{ns-2} \right) \left\{ M(p, 1) \right\}^{s-1}$$

if $n > 2$.

$$\left\{ M(p, R) \right\}^s \leq \left(1 + \frac{R^{2s} - 1}{k^2} \right) \frac{(2|a_2|k^2 + |a_1|)}{2|a_2|(1+k^2) + 2|a_1|} \left\{ M(p, 1) \right\}^s$$

$$- s|a_1| \left(\frac{R^{2s} - 1}{2s} - \frac{R^{2s-1} - 1}{2s-1} \right) \left\{ M(p, 1) \right\}^{s-1}$$

if $n = 2$,

Further, Corollary 1.1 is an improvement of Theorem A proved by Dewan and Ahuja [2].

Remark. 1.2. An interesting aspect of our theorem is that we estimate an upper bound of $\left| \left\{ p(R e^{i\theta}) \right\}^s - \left\{ \beta p(r e^{i\theta}) \right\}^s \right|$ obtained in terms of the growths of the polynomial on two circles of radii r such that $1 \leq r \leq R$ and 1. Moreover, the quantity $\left| \left\{ p(R e^{i\theta}) \right\}^s - \left\{ \beta p(r e^{i\theta}) \right\}^s \right|$ can be interpreted geometrically as the modulus of the difference of the values of the s^{st} power, s any positive integer, of the polynomial $p(z)$ concerned and the coefficient-perturbed polynomial $\beta p(z)$ obtained from $p(z)$ by multiplying every coefficient by an arbitrary complex number β , respectively evaluated at the corresponding points where an arbitrarily fixed ray from the origin of the complex plane intercepts on two concentric circles of radii R and r , where $1 \leq r \leq R$, centered at the origin. It is worth to note that polynomial $p(z)$ and its perturbed counterpart $\beta p(z)$ have the same set of zeros on the circle $|z|=k, k \leq 1$.

Remark. 1.3. When we assign $s=r=1$ and $\beta=0$ in our theorem we get the following which is an improvement of a result of Dewan and Ahuja [2, Corollary 3].

Corollary 1.2. If $p(z) = \sum_{v=0}^n a_v z^v$ is a polynomial of degree $n \geq 2$ having all its zeros on $|z|=k, k \leq 1$, then for $R \geq 1$,

$$M(p, R) \leq \left(1 + \frac{R^n - 1}{k^n}\right) \frac{(n|a_n|k^2 + |a_{n-1}|)}{n|a_n|(1+k^2) + 2|a_{n-1}|} M(p, 1) - s|a_1| \left(\frac{R^n - 1}{n} - \frac{R^{n-2} - 1}{n-2}\right)$$

if $n > 2$,

$$M(p, R) \leq \left(1 + \frac{R^2 - 1}{k^2}\right) \frac{(2|a_2|k^2 + |a_1|)}{2|a_2|(1+k^2) + 2|a_1|} M(p, 1) - s|a_1| \left\{\frac{R^2 - 1}{2} - (R-1)\right\}$$

if $n = 2$.

Remark. 1.4. When we set $k = s = r = 1$ and $\beta = 0$ in the theorem, we get the following improved version of a result of Dewan and Ahuja [2, Corollary 2] which further gives the parallel improved match of inequality(1.2) due to Ankeny Rivlin [1], in case all the zeros of the polynomial lie on the unit circle.

Corollary 1.3. If $p(z)$ is a polynomial of degree n having all its zeros on $|z|=1$, then for $R \geq 1$,

$$M(p, R) \leq \frac{R^n + 1}{2} M(p, 1) - s|a_1| \left(\frac{R^n - 1}{n} - \frac{R^{n-2} - 1}{n-2}\right) \text{ if } n > 2,$$

and

$$M(p, R) \leq \frac{R^2 + 1}{2} M(p, 1) - s|a_1| \left\{\frac{R^2 - 1}{2} - (R-1)\right\} \text{ if } n = 2.$$

2. LEMMA

The following lemmas are needed for the proof of the theorem.

Lemma 2.1. If $p(z) = \sum_{v=0}^n a_v z^v$ is a polynomial of degree n having all its zeros on the circle $|z|=k, k \leq 1$, then

$$M(p', 1) \leq \frac{n}{k^n} \left\{ \frac{n|a_n|k^2 + |a_{n-1}|}{n|a_n|(1+k^2) + 2|a_{n-1}|} \right\} M(p, 1) \tag{2.1}$$

This lemma was by Dewan and Mir [3].

Lemma 2.2. If $p(z) = \sum_{v=0}^n a_v z^v$ is a polynomial of degree n , then for $R \geq 1$ $M(p, R) \leq R^n M(p, 1) - (R^n - R^{n-2})|a_0|$, if $n > 1$,

$$\tag{2.2}$$

and

$$M(p, R) \leq R M(p, 1) - (R-1)|a_0|, \text{ if } n = 1. \tag{2.3}$$

The above results were due to Frappier et.al [4].

Lemma 2.3. If $T > 0$ is any constant then for $t > 0$ the function

$$f(t) = 1 - T(1-t^{-2}) \tag{2.4}$$

is non-increasing function of t .

Proof of Lemma 2.3. The proof is simple and is implied, for example, by derivative test.

Proof of the Theorem

We first prove inequality (1.5). By hypothesis $p(z)$ is a polynomial of degree n having all its zeros on $|z|=k, k \leq 1$ and by applying Lemma 2.1, we have

$$M(p', 1) \leq \frac{n}{k^n} \left\{ \frac{n|a_n|k^2 + |a_{n-1}|}{n|a_n|(1+k^2) + 2|a_{n-1}|} \right\} M(p, 1) \text{ for } |z|=1. \tag{3.1}$$

For each $\theta, 0 \leq \theta < 2\pi, 1 \leq r \leq R$, any complex number β and any positive integer s , we have

$$\begin{aligned} \{p(R e^{i\theta})\}^s - \{\beta p(r e^{i\theta})\}^s &= (1 - \beta^s) \{p(r e^{i\theta})\}^s \\ &+ \{p(R e^{i\theta})\}^s - \{p(r e^{i\theta})\}^s. \end{aligned} \tag{3.2}$$

which implies

$$\left| \left\{ p\left(R e^{i\theta} \right) \right\}^s - \left\{ \beta p\left(r e^{i\theta} \right) \right\}^s \right| \leq \left| 1 - \beta^s \right| \left\{ M(p, r) \right\}^s + \left| \left\{ p\left(R e^{i\theta} \right) \right\}^s - \left\{ p\left(r e^{i\theta} \right) \right\}^s \right| \tag{3.3}$$

$$\begin{aligned} \left\{ p\left(R e^{i\theta} \right) \right\}^s - \left\{ p\left(r e^{i\theta} \right) \right\}^s &= \int_r^R \frac{d}{dt} \left\{ p\left(t e^{i\theta} \right) \right\}^s dt \\ &= \int_r^R s \left\{ p\left(t e^{i\theta} \right) \right\}^{s-1} p'\left(t e^{i\theta} \right) e^{i\theta} dt, \end{aligned}$$

from which it is implied that

$$\left| \left\{ p\left(R e^{i\theta} \right) \right\}^s - \left\{ p\left(r e^{i\theta} \right) \right\}^s \right| \leq s \int_r^R \left| p\left(t e^{i\theta} \right) \right|^{s-1} \left| p'\left(t e^{i\theta} \right) \right| dt \tag{3.4}$$

As $p(z)$ is a polynomial of degree $n > 2$, the polynomial $p'(z)$ is of degree $n - 1 \geq 2$, therefore applying the same inequality (2.2) of Lemma 2.2 to both $p(z)$ and $p'(z)$, we have for any $t \geq 1$ and $0 \leq \theta < 2\pi$

$$\left| p\left(t e^{i\theta} \right) \right| \leq t^n M(p, 1) - (t^n - t^{n-2}) |a_0| \tag{3.5}$$

and

$$\left| p'\left(t e^{i\theta} \right) \right| \leq t^{n-1} M(p', 1) - (t^{n-1} - t^{n-3}) |a_1| \tag{3.6}$$

Inequality (3.4) in conjunction with inequalities (3.5) and (3.6) gives

$$\begin{aligned} \left| \left\{ p\left(R e^{i\theta} \right) \right\}^s - \left\{ p\left(r e^{i\theta} \right) \right\}^s \right| &\leq s \int_r^R \left\{ t^n M(p, 1) - (t^n - t^{n-2}) |a_0| \right\}^{s-1} \\ &\quad \times \left\{ t^{n-1} M(p', 1) - (t^{n-1} - t^{n-3}) |a_1| \right\} dt \\ &= s \int_r^R \left\{ t^n M(p, 1) \right\}^{s-1} \left\{ 1 - (1 - t^{-2}) \frac{|a_0|}{M(p, 1)} \right\}^{s-1} \\ &\quad \times \left\{ t^{n-1} M(p', 1) - (t^{n-1} - t^{n-3}) |a_1| \right\} dt \end{aligned} \tag{3.7}$$

By (2.4) of Lemma 2.3, the function $1 - (1 - t^{-2}) \frac{|a_0|}{M(p, 1)}$ is a non-increasing function of $t > 0$ and, in particular, for $1 \leq r \leq t$, we have

$$1 - (1 - t^{-2}) \frac{|a_0|}{M(p, 1)} \leq 1 - (1 - r^{-2}) \frac{|a_0|}{M(p, 1)} \tag{3.8}$$

Inequality (3.7) on using (3.8) becomes

$$\begin{aligned} \left| \left\{ p\left(R e^{i\theta} \right) \right\}^s - \left\{ p\left(r e^{i\theta} \right) \right\}^s \right| &\leq s A^{s-1} \int_r^R \left\{ t^n M(p, 1) \right\}^{s-1} \\ &\quad \times \left\{ t^{n-1} M(p', 1) - (t^{n-1} - t^{n-3}) |a_1| \right\} dt \end{aligned}$$

where

$$A = 1 - \left(1 - \frac{1}{r^2} \right) \frac{|a_0|}{M(p, 1)}$$

Using inequality (3.1) for $M(p', 1)$ in the above inequality, we obtain

$$\begin{aligned} \left| \left\{ p\left(R e^{i\theta} \right) \right\}^s - \left\{ p\left(r e^{i\theta} \right) \right\}^s \right| &\leq s A^{s-1} \int_r^R \left\{ t^n M(p, 1) \right\}^{s-1} \\ &\quad \times \left[t^{n-1} \frac{n}{k^n} \left\{ \frac{n |a_n| k^2 + |a_{n-1}|}{n |a_n| (1 + k^2) + 2 |a_{n-1}|} \right\} M(p, 1) - (t^{n-1} - t^{n-3}) |a_1| \right] dt \\ &= s A^{s-1} \left\{ M(p, 1) \right\}^{s-1} \\ &\quad \times \int_r^R \left[t^{ns-1} \frac{n}{k^n} \left\{ \frac{n |a_n| k^2 + |a_{n-1}|}{n |a_n| (1 + k^2) + 2 |a_{n-1}|} \right\} M(p, 1) - (t^{ns-1} - t^{ns-3}) |a_1| \right] dt \\ &= A^{s-1} \left[\left\{ M(p, 1) \right\}^s \frac{(R^{ns} - r^{ns})}{k^n} \frac{(n |a_n| k^2 + |a_{n-1}|)}{n |a_n| (1 + k^2) + 2 |a_{n-1}|} \right. \\ &\quad \left. - s |a_1| \left(\frac{R^{ns} - r^{ns}}{ns} - \frac{R^{ns-2} - r^{ns-2}}{ns-2} \right) \left\{ M(p, 1) \right\}^{s-1} \right] \end{aligned} \tag{3.9}$$

Combining (3.3) and (3.9), the desired result follows.

Next, inequality (1.6) is proved.

Since $p(z)$ is a polynomial of degree $n = 2$, the polynomial $p'(z)$ is of first degree and therefore applying inequalities (2.2)

and (2.3) of Lemma 2.2 respectively to $p(z)$ and $p'(z)$, we have for any $t \geq 1$ and $0 \leq \theta < 2\pi$

$$\left| p(te^{i\theta}) \right| \leq t^2 M(p, 1) - (t^2 - 1) |a_0|, \quad (3.10)$$

and

$$\left| p'(te^{i\theta}) \right| \leq tM(p', 1) - (t-1) |a_1|. \quad (3.11)$$

The proof of this part follows on the same lines as that of inequality (1.5), but instead of using inequalities (3.5) and (3.6), we use respectively the above inequalities (3.10) and (3.11).

Hence the proof of the theorem is complete.

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