

*view Article*  
**Medicinal Uses of Mannich Bases**

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**Introduction**

The Mannich Reaction is used in the synthesis of natural products and pharmaceuticals. Therefore in this review we discuss the medicinal uses of Mannich bases with examples in the medicinal field. A large number of different bioactivities of Mannich bases are anticonvulsant, antimalarial, anticancer, analgesic and antimicrobial drugs. Also Mannich bases are used as prodrugs.

**Application**

The Mannich reaction is one of the most important C-C bond formation

methods in organic synthesis (Sharifi, *et. al* , 2001). The Mannich-reaction is employed in the organic synthesis of natural compounds like, for instance, peptides, nucleotides, antibiotics and alkaloids. Other application are in agrochemicals such as plant growth regulators, paint and other polymer chemistry, catalysts and crosslinking and is used in the synthesis of medicinal compounds (Dimmock, 1997).

**Key word: Mannich reaction, medicinal uses, prodrugs**

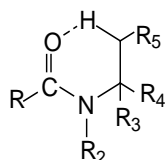
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## Prodrug uses

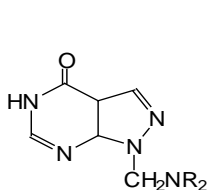
The Mannich bases are used as potential prodrugs of NH-acidic compounds. Interamolecular hydrogen bonding between the amine proton and the carbonyl

oxygen hinders the solvation of the polar group of molecule and the solubility of drugs increases (**Guarino, and Stella 2004; Jezierska and Panket, 2007**).

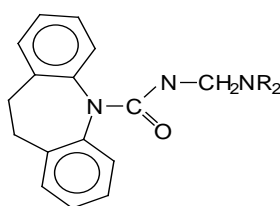


Dissolution rate for drugs Allopurinol (**1**), Carbamazepine (**2**) and Rolitetracycline (**3**), was

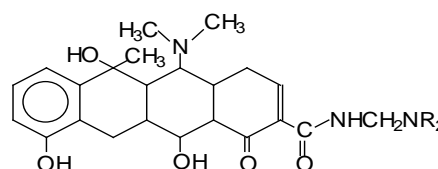
improved using N-Mannich bases derivatization (**Guarino, and Stella, 2004**).



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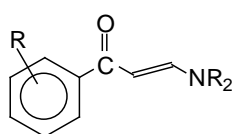


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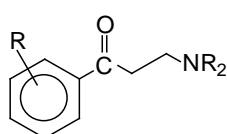
## Anticancer activity

A series of mono Mannich bases derived from acetophenone like 1-aryl-5-dimethylamino-1-penten-3-one hydrochloride (**4**), and 1-aryl-3-diethylamino-1-propane

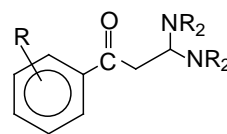
hydrochloride (**5**), and corresponding bis-Mannich bases (**6**) were synthesized as an anti-cancer agent (**Dimmock. et-al 1998; Gul, et. al , 2000**).



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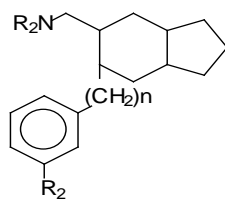


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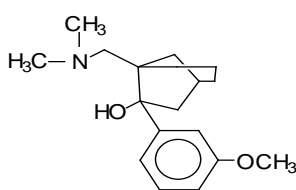
### Analgesic activity

$\beta$ -amino ketones like  $\alpha$ -alkyl- $\beta$ -dimethylaminopropiophenone (Daruwala, *et. al* , 1974),  $\beta$ -amino ketones derived from 1-(N-p-hydroxyethyl-4-piperidyl)-3-(4-piperidyl) propane (Varma and Obles, 1968), a series of 6(alkylamino)methylhexahydro-5-

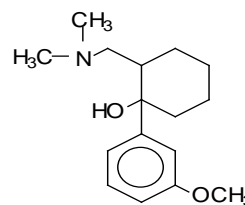
arylmethanoindan-5-ols(7) alkyl-4,7-methanoindan-5-ols(8) Tramadol(9), (Aboul-enein 1993) a series of 3-{1-[4'-carbethoxy-4'-(R-) phenyl]-piperidino-propiofenones (10), (Janssen, *et. al* , 1959) exhibited slight analgesic effect.



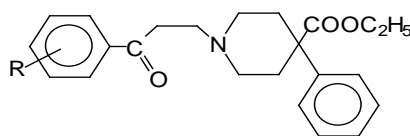
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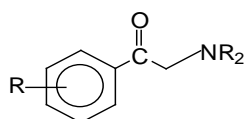


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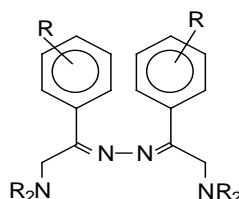
### Anticonvulsant activity

Mono-Mannich bases 3-amino-1-aryl-propanone (11) , N,N'-bis(3-amino-1-aryl-propylidene)hydrazine (Gul, *etal*, 2002), (12) and

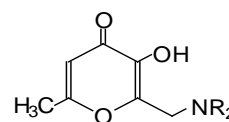
3-hydroxy-6-methyl-2-aminomethyl 4H-pyran (13), (Aytemir, 2007), were synthesized as anticonvulsant agent.



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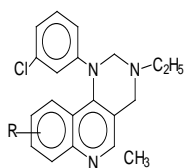
### Antimalarial

1-(3-chlorophenyl)-3,9-dimethyl-3-ethyltetrahydropyrimido[5,4c]quinoline (14), (Nasr, *et. al*, 1978), novel

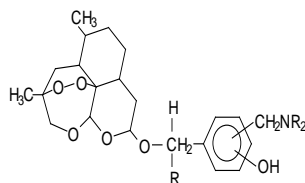
artemisinin derivatives bearing Mannich base (15) (Li, *et. al*, 2003), new series of 4-aminoquinoline Mannich base derivatives (16) (Raynes, *etal*, 1999) and series of 4-

[(7-chloro-4-quinoliny]amino]-2-  
 [(di-ethylamino)methyl]-6-  
 alkylphenols (**17**) (**Kesten, et al,**

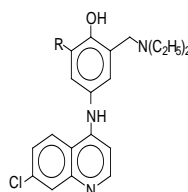
**1987**) were synthesized as anti-  
 malaria agents.



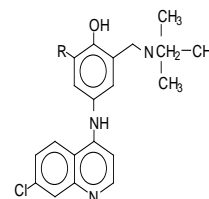
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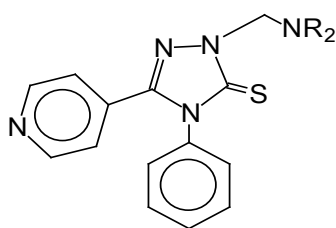


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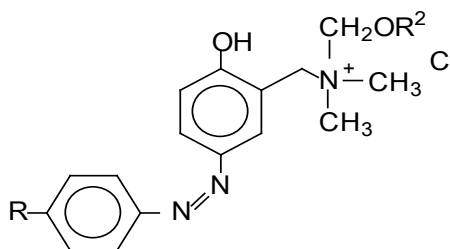
## Antimicrobial

Mannich base derivatives of 4-  
 phenyl-5-pyridin-4-yl-4H-1,2,4-  
 triazole-3-thiol (**18**) (**Bayrak, et al,**  
**2008**), alkoxymethyl-dimethyl{2-  
 hydroxy-5-[(4-X-

phenyl)azo]benzyl}ammonium  
 chlorides, (**19**) (**Pernak, and**  
**Kmiecik, 1999**) were synthesized as  
 antimicrobial agents.



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## Conclusion

In this work we reviewed the  
 medicinal uses of Mannich bases

and we summarized the biological  
 activities of the Mannich bases in  
 medicinal field with examples.

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