www.pharmaerudition.org

ISSN: 2249-3875

International Journal of Pharmaceutical Erudition

Research for Present and Next Generation

MAY 2019

Vol: 09 Issue:1

(7-14)

ISSN 2249-3875

International Journal of Pharmaceutical Erudition

Research Paper

ANTI DIABETIC ACTIVITY OF 1,2 - NAPHTHOQUINONE

Bansal M. and Sharma Anurag

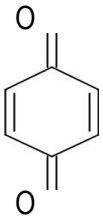
Sambalpur University, Orissa, India 768019

The popular experimental models -Alloxan-induced *diabetes* and Streptozotocin-induced *diabetes*- however, could not be used because in these models the induced diabetes is due to destruction of β-cells of islet of Langerhans in pancreas, therefore reducing the levels of circulating insulin leading to hyperglycemia. On the contrary, the synthesized compounds were to be tested against Type 2 diabetes. On the contrary, the synthesized compounds were supposed to be tested against Type 2 diabetes; the anti-hyperglycemic ability of synthesized compounds was envisaged to be established by their ability to increase sensitivity of peripheral tissues to circulating insulin in the animals. Hence, it was thought worth to validate and use a reported ethanol-induced diabetic model in rats, which would definitely examine the anti-hyperglycemic activity of the synthesized compounds, and also their anti-diabetic potential, especially for treating Type 2 diabetes. According to Synthetic Scheme compounds were synthesized from IIa to IIId and Compound purity checked by TLC, Melting Point and FTIR studies. All the compound according to characterization by IR were found appropriately with the presence of functional group and further next derivative will processed in next step.

Key Words ; anti-hyperglycemic activity, Type 2 diabetes, TLC, FTIR.

INTRODUCTION

Quinones are described as a class of cyclic organic compounds comprising of a six-membered unsaturated ring to which two oxygen atoms are bonded as carbonyl groups. The name quinone is applied to the whole group, but it is often used specifically to refer to (1) p-benzoquinone (Fig.1) is also known but the meta-isomer does not exist.



(1)

Fig. 1: Structure of p-benzoquinone (1)

This structure plays an important role in theories of chemical structure and color, since quinones occur as pigments in bacteria, fungi, and certain higher plants; animals containing quinones obtain them from plants they eat. Quinones are obtained in the form of colored crystals, which have a sharp odor. For example, para-benzoquinone (4), with a melting point of 116°C, and 1,4-naphthoquinon [1]. (5), with a melting point of 128.5°C, are yellow, while ortho-benzoquinone (3), **(Fig.1)** with a melting point of 70°–80°C (with decomposition), and anthraquinone are red. Quinonoids compounds are widely distributed in nature, mainly as secondary metabolites, in all respiring animal and plant cells. Some of these quinones can act as vital links in the electron transport chain playing important roles in the bio-chemistry of energy production in their natural hosts, while many others

show pronounced cytotoxic and allergic actions that might enable the hosts to define themselves against invading pathogens. A number of natural quinonoids as well as their synthetic analogues have been found to possess significant antitumor activity by virtue of their facile redox cycling capacity. Incidentally, quinonoids comprise the second largest class of antitumor agents currently in use, e.g. the daunomycin group of drugs based on anthracyclin antibiotics (Powis 1987). Recent studies have been demonstrated that this drug, kill tumor cells through apoptosis and has been recognized as a target for cancer therapy. Various pigments in nature are derivatives of quinones; for example, muscapharin, the dye substance of the fly agaric, is a derivative of para-benzoquinone. Quinones are readily reduced to yield diatomic phenols [for example, in industry, hydroquinone is obtained from (I) in this way]. They actively enter in diene synthesis, as well as form molecular complexes with phenols. They are also used in analytical chemistry.

Main objective is to search the potent compounds for various pharmacological activities with lesser adverse effect.

The literature survey has presented comprehensive detail analogues, potent heterocyclic compounds reported for particular pharmacological activity and the method or technique involved in evaluation process.

After literature survey of Napthaquinone moieties showed promising anti-oxidant and anti-diabetic activities.

To establish the method of synthesis for the proposed compounds.

To synthesize the title compounds by appropriate methods.

To carryout the preliminary tests such as physical constant determination, solubility, TLC etc.

To confirm the structures of the synthesized compounds by IR, NMR and elemental analysis calculated.

To evaluate the proposed compounds for their anti-diabetic activity. As a result of remarkable pharmacological efficiency of Napthaquinone moieties, intensive research has been focused on anti-diabetic activity.

To achieve the synthesis of substituted Napthaquinone derivatives.

The purity and progress of the reactions will be monitored by TLC.

The purification of the compounds will be carried out by recrystallization using suitable solvents.

To characterize the structures of newly synthesized compounds by UV, IR, NMR, elemental analysis and MASS spectra.

To evaluate the anti-diabetic activity of new compounds by standard protocols to study the structure-activity relationships and to optimize the structure.

So conclusion from literature review studies: The following requirement must be essential for anti-diabetic activity.

1. Napthaquinone Moiety.
2. Substituted electron withdrawing group at 3rd Position.(Substitution=, OH, Alkoxy)

ISSN 2249-3875

International Journal of Pharmaceutical Erudition

3. Substituted at 7th position (substitution = NH_2, NO_2, C_2H_5, OCH_3, CH_3)

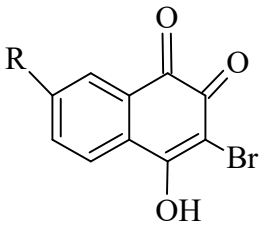


Fig. 2: Target Molecule

Where R= NH_2, NO_2, C_2H_5, OCH_3, CH_3

EXPRIMENTAL WORK

Introduction:

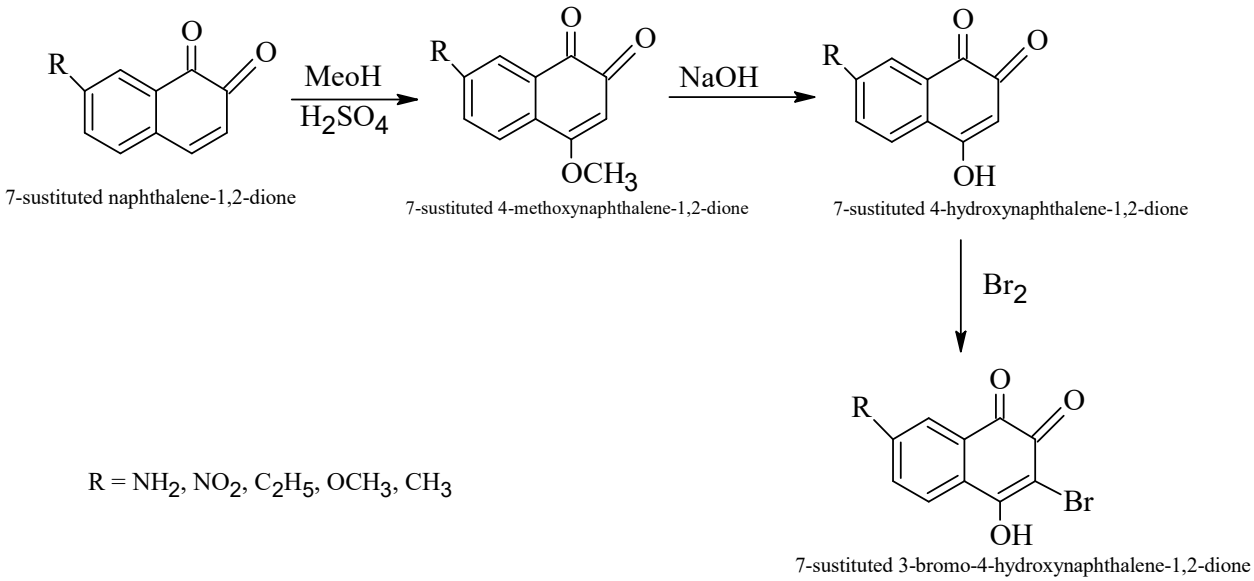
The identification and characterization of the compound were carried out by the following procedure to as certain that all prepared compounds were of different chemical nature, than the respective parent compound.

1. Melting Point
2. Solubility
3. Thin Layer Chromatography
4. I.R
5. ^1H -NMR
6. Mass spectrometry.

All the melting points were determined by melting point apparatus and boiling points were determined by capillary method in paraffin bath and are uncorrected.

- The chemicals employed in the synthetic work were provided by our college.
- UV/Visible spectra were run on JASCO / SHIMANDZU spectrophotometer.
- FTIR spectra were recorded in KBr powder on a Jasco V460 IR Spectrometer by diffused Reflectance technique.
- 1H- NMR spectra were measured in d6-DMSO on a Bruker II Avance 400 MHz NMR spectrometer. The reported chemical shifts were against TMS.
- Mass spectra were recorded on a JEOL JMS600 spectrum.

Synthetic scheme:



7-sustituted naphthalene-1,2-dione

7-sustituted 4-methoxynaphthalene-1,2-dione

7-sustituted 4-hydroxynaphthalene-1,2-dione

R = NH_2, NO_2, C_2H_5, OCH_3, CH_3

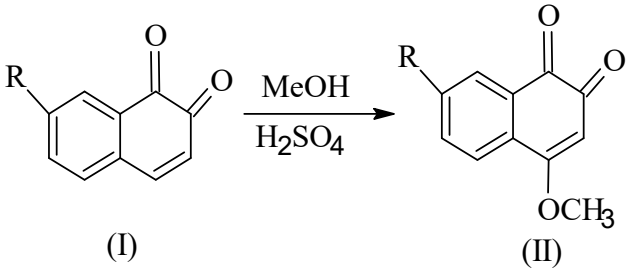
7-sustituted 3-bromo-4-hydroxynaphthalene-1,2-dione

ISSN 2249-3875

International Journal of Pharmaceutical Erudition

Synthetic Procedure:-

Step 1:- Synthesis of 7-substituted 4-methoxy naphthalene-1,2-dione



(I) (II)

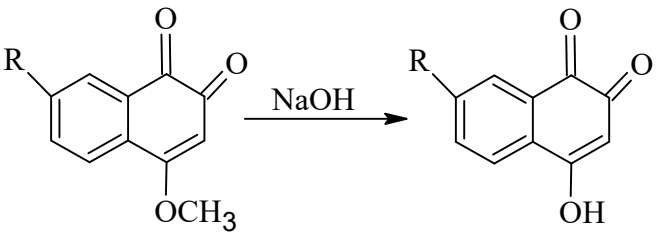
[Comp-II]

A 7-substituted 1,2-napthaquinone COMP-I (0.005 mole) in methanol (3.6 mL) and H_2SO_4 (1 mL) was added slowly to a well stirred .The reaction mixture was stirred for further 2 h. The crude product was filtered off, dried well and crystallized from the appropriate solvent to give compounds COMP-II to obtain pure product of 95.02 % w/w yield having m.p.-80-82 ºC.

Table 1: Analysis of 7-substituted 4-methoxy naphthalene-1,2-dione (IIa-d)

Comp. Code	Mol. Formula	Melting point Range (ºC)	% yield	Rf value
IIa	$C_{11}H_9NO_3$	267-268	85.23	0.42
IIb	$C_{11}H_7NO_5$	243-244	76.62	0.70
IIc	$C_{13}H_{12}O_3$	239-240	66.62	0.59
IId	$C_{12}H_{10}O_4$	254-255	87.77	0.81

Step 2:- Synthesis of 7-substituted 4-methoxy naphthalene-1,2-dione



(II) (III)

To a suspension of COMP-II (1.12 g, 5 mmol) in

Table 2: Analysis of 7-substituted 4-methoxy naphthalene-1,2-dione(IIIa-d)

Comp. Code	Mol. Formula	Melting point Range (ºC)	% yield	Rf value
IIIa	$C_{10}H_7NO_3$	256-257	63.03	0.78
IIIb	$C_{10}H_5NO_5$	290-291	77.62	0.51
IIIc	$C_{12}H_{10}O_3$	278-279	59.11	0.56
IIId	$C_{11}H_8O_4$	251-252	65.23	0.67

ISSN 2249-3875

International Journal of Pharmaceutical Erudition

NaOH solution (25 ml, 4:1 V) was added. The reaction mixture was refluxed for 6 h then left to cool at room temperature. The obtained solid product was filtered off, dried and crystallized from ethanol to give compound III.

RESULT & DISCUSSION

Physical and Spectral Characteristics

Physical Characteristics

All the synthesized compounds were off white, light yellow to brown colored crystalline solids. All the compounds are freely soluble in dimethylsulfoxide and other solvents like methanol, ethanol. The melting point of the compounds was in the range of 236ºC to 296ºC.

Spectral Characteristics

IR spectra

IR spectra of all compounds were recorded on FT-IR 8400S Shimadzu spectrophotometer using KBr. All the synthesized compounds have shown characteristic stretching and bending in desired range.

Mass spectra

Mass spectra were obtained using. All the spectra were taken by direct infusion mass with ESI and APCI in positive and negative mode of ionization ranging from 200-500 m/e. All the compounds possess a molecular ion M+, M+1 peak.

^{1}H NMR spectra

The ^{1}H NMR spectra of some of the compounds were studied in d6-DMSO on a Bruker II Avance 400 MHz NMR spectrometer. All the compounds show characteristic chemical shift from TMS in terms of δ ppm. δ value obtained in the desired range which signifies the presence of aromatic ring.

SYNTHESIZED COMPOUNDS:-

Physical and Spectral Characteristics of 7-substituted 4-methoxy naphthalene-1,2-dione: (comp-IIa-d)

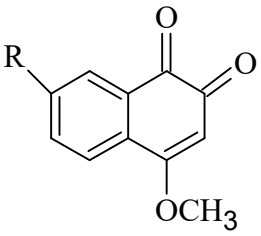


Fig. 3: (Comp- IIa-d)
R= NH_2, NO_2, C_2H_5, OCH_3

Table 3:-Physical Characteristics of comp-IIa-d

Comp. Code	Mol. Formula	Melting point Range (^{0}C)	% yield	Rf value
IIa	$C_{11}H_9NO_3$	267-268	85.23	0.42
IIb	$C_{11}H_7NO_5$	243-244	76.62	0.70
IIc	$C_{13}H_{12}O_3$	239-240	66.62	0.59
IId	$C_{12}H_{10}O_4$	254-255	87.77	0.81

Solvent system for TLC- Methanol: Ethyl acetate: Toluene (3:4:3)

ISSN 2249-3875

International Journal of Pharmaceutical Erudition

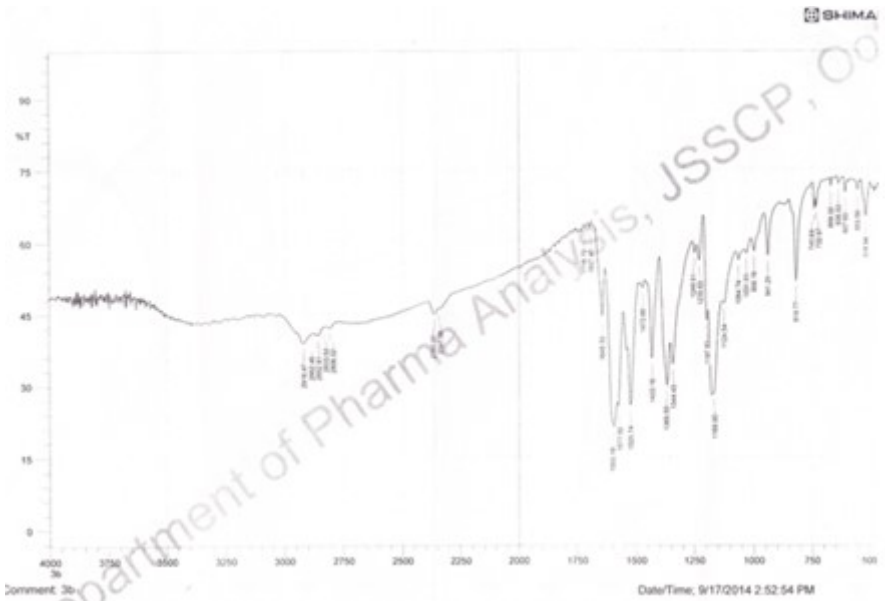


Fig. 4: IR Spectra of comp-IIa

Table 4:-Spectral Characteristics of IIa

Fun. group assigned	Group frequency in Wave number (cm^{-1})
Aromatic C-H	2833.52,2806.52
Stretch C=C	1645.33
Stretch C-N	1064.74, 1168.90
Stretch CH_2	2916.47,2882.46

Physical and Spectral Characteristics of 7-substituted 4-methoxy naphthalene-1,2-dione: (complIIa-d)

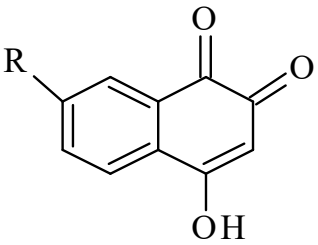


Fig. 5: (Comp- IIIa-d)
R= NH_2, NO_2, C_2H_5, OCH_3

Table 5 : Physical Characteristics of comp-IIIa-d

Comp. Code	Mol. Formula	Melting point Range (^0C)	% yield	Rf value
IIIa	$C_{10}H_7NO_3$	256-257	63.03	0.78
IIIb	$C_{10}H_5NO_5$	290-291	77.62	0.51
IIIc	$C_{12}H_{10}O_3$	278-279	59.11	0.56
IIId	$C_{11}H_8O_4$	251-252	65.23	0.67

Solvent system for TLC- Methanol: Ethyl acetate: Toluene (3:4:3)

ISSN 2249-3875

International Journal of Pharmaceutical Erudition

(Fig. 6: IR Spectra of comp-IIIa)

Table 6:-Spectral Characteristics of comp-IIIa

Fun. group assigned	Group frequency in Wave number (cm^{-1})
Aromatic C-H	2956.97, 2920.32
Stretch C=C	1649.19
Stretch C-N	1303.92
Stretch CH_3	3009.05, 3061.13,3090.07
Stretch NH_2	3365.90
C-S-C starching due to overtone	650.03

CONCLUSION:

On the contrary, the synthesized compounds were supposed to be tested against *Type 2 diabetes*; the anti-hyperglycemic ability of synthesized compounds was envisaged to be established by their ability to increase sensitivity of peripheral tissues to circulating insulin in the animals. Hence, it was thought worth to validate and use a reported ethanol-induced diabetic model in rats, which would definitely examine the anti-hyperglycemic activity of the synthesized compounds, and also their anti-diabetic potential, especially for treating Type 2 diabetes.

According to Synthetic Scheme compounds were synthesized from IIa to IIId and Compound purity chacked by TLC and Melting Point and FTIR studies. All the compound according to characterization by IR were found appropriately with the presence of functional group and further next derivative will processed in next step.

REFERENCE

1. Brown, H.C., et al., in Baude, E.A. and Nachod, F.C., Determination of Organic Structures by Physical Methods, Academic Press, New York, 1955.

2. Gilchrist, Thomas Lonsdale; Gilchrist, T. L. (1997). Heterocyclic chemistry. New York: Longman. ISBN 0-582-27843-0.

ISSN 2249-3875

3. Joule, John A.; Mills, Keith, eds. (2010). Heterocyclic Chemistry (5th ed). Oxford: Wiley. p. 250. ISBN 978-1-405-13300-5.

4. Lagoja, Irene M. (2007). "Pyrimidine as Constituent of Natural Biologically Active Compounds". Chemistry and Biodiversity 2 (1):150.

5. Grimaux, E. (1879). "Syntheses des dérivésuriques de la série de l'alloxane".Comptesrendushebdomadaires des séances de l'Académie des Sciences 88: 85–87.