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Ethno Med, 17(1-2): 57-69 (2023)
PRINT: ISSN 0973-5070 ONLINE: ISSN 2456-6772
DOI: 10.31901/24566772.2023/17.1-2.654

A Meta-analysis of the Efficacy of Homoeopathic Ultra High Dilutions on Wheat Plant Growth and Disease Management

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KEYWORDS Agriculture. Crop Protection. Germination. Homoeopathy. Plants

ABSTRACT Homeopathic medicines have been examined in plant models for various purposes like promotion of seed germination, growth and physiology of plants, plant disease control, secondary metabolites enhancement, metal detoxification, etc. However, a limited number of the studies question the reliability of the data, which restricts the use of homoeopathy in the plant system. Therefore this meta-analysis was undertaken to investigate the effect of various homoeopathic medicines on seed germination, growth and disease control in wheat (*Triticumaestivum L.*). A web search was performed on the National Library of Medicine's PubMed search engine and 16 studies were retrieved based on inclusion and exclusion criterions. Using data from each study, two by two tables were prepared and fixed mean differences for plant growth, odd ratios for seed germination and risk ratio for disease control along with their ninety-five percent confidence intervals were calculated by Inverse Variance method using Review Manager 5.4.1 (Rev Man 5.4.1) software. Data suggests that gibberellic acid significantly reduces the wheat seedling/stalk growth in autumn season with mean difference of -3.99 (95% CI: -4.41, -3.51), with inconsistent effect in winter and spring season. Further, Arsenicum album treatment promoted the seedling growth in wheat with mean difference: 11.86 (95% CI: 11.67, 12.06), while there was no significant effect on seed germination, and odd ratio: 1.27 (95% CI: 0.87, 1.85, P = 0.22). Moreover, various homoeopathic agents significantly reduced the risk of *Fusarium* and *Alternaria* infection in wheat seeds. To conclude, meta-analysis of included studies suggests significant effects of homoeopathic agents in various aspects of wheat plant growth and disease management.

INTRODUCTION

Homoeopathic treatment is based on the principle of Similia Similibus Curentur, which includes therapeutic similarity, pathogenetic examination of medicines on healthy individuals and patient's symptom-based selection and use of ultra-high dilutions. However, due to its unconventional assumptions, homoeopathy and its specificities and supporting evidence are not fully approved by the medical and scientific community (Teixeira 2011). Nevertheless, multiple experimental studies have been performed in various models including humans, animals, plants, cell line cultures, etc. to determine the efficacy of homoeopathic medicine (Senel 2019). Among these studies, research on plant models has multiple advantages including big sample size and datasets, short duration, low cost, no need of placebo effect and absence of ethical hurdles, which are applied to animal and human research (Baumgartner et al. 2008).

Homoeopathic medicines have been examined in plant models for various purposes like inhibition of pathogens and pests, enhancement of secondary metabolites, metal detoxification, promoting seed germination, growth and physiology of plants (Toledo et al. 2011). It has been reported that drugs like *Dryopteris filix-mas* (*L.*) *Schott* and Blatta Orientalis can completely inhibit the *Fusarium oxysporum* population in the seed of wheat plants (Khanna et al. 1989). Further, homoeopathic drugs have been shown to induce seed germination and plant growth in various species (Majewsky et al. 2014; Santos et al. 2011; Sukul et al. 2009; Baumgartner et al. 2008; Sukul et al. 2008; Baumgartner et al. 2004; Brizzi et al. 2000; Betti et al. 1994). Similarly, Khanna and Chandra (1976) reported that use of Kali iodide and *Thuja occidentalis* L. can control the tomato rot caused by *Fusarium roseum*. Further, use of Sulphur against growth of aflatoxins producing fungi, *Aspergillus parasiticus*, Lachesis and *Chimaphila umbellate* (L.) against tobacco mosaic virus and Kali iodide against powdery mildew of tomato were found to be beneficial for control of these pathogens (Rolim et al. 2005; Sinha et al. 1983; Verma et al. 1969). Ramírez- Rodríguez et al. (2022) conducted a study on strawberry plants to control red spider mite and he found that the homoeopathic remedy *Lycoperdon bovista* Pers. and *Atropa belladonna* L. both at 6 CH and 30 CH showed better efficacy and reduced the mite infection on strawberry plants.

A study was conducted by Ferreira et al. (2021) to assess the effect of *Artemisia maritime*. (*A. cina*) on nematode (Meloidogyne) growth, which parasitises the lettuce. It was found that Cina can be used as complementary treatment for Meloidogyne nematode control.

Nunes et al. (2021) conducted a study on *Hypericum perforatum* L. to assess the efficacy of homoeopathic medicine on the vegetative growth. Through this study it was found that *Silicea terra*, Kali carbonicum, Natrum muriaticum and Phosphorus increased the vegetative growth. However, systematic pathogenetic trials of homoeopathy using plants are very few leading to limited information about homoeopathic material medica specific for plants, which is required for the identification of individualised homoeopathic medicines for each plant species and disease type. Limited number of the studies also put a question mark on reliability of the data.

In the current study, the researchers performed a specific meta-analysis effect of selective homoeopathic medicines on wheat plant growth and disease management. The meta-analysis represents the effect size of most frequently studied homoeopathic medicines in the wheat plant model and provides critical insights for their use in management of wheat plant growth and diseases.

Objectives

Primary Objective

The primary objective of this study is to review the efficacy of specific homoeopathic medicines on growth and germination parameters of wheat (*Triticum aestivum L.*) plants.

Secondary Objectives

The secondary objectives of this study are:

1. To review the mechanism of action of selective homoeopathic medicines on seed germination/growth of wheat plants.
2. To review the commonest pests or pathogens that infest wheat plants and the forerunners amongst homoeopathic medicines for each individual pest.

METHODOLOGY

Study Selection

The criteria for a study to be in this meta-analysis were that it must include wheat as the plant model, it must involve use of one or more homoeopathic treatments, it should have empirical data either on plant growth or disease control, and it should be from a peer reviewed English language scientific journal.

The excluded articles were those which were not related to wheat as the plant model, did not involve homoeopathic medicine, did not possess empirical data either on plant growth or disease control, and were in a language other than English.

Search Strategy

A web search was performed on the National Library of Medicine's PubMed search engine for all empirical studies associated with use of homoeopathy in the wheat plant model (from inception until 2021). The researchers searched the keywords "homoeopathic treatment", "wheat", "wheat plant growth" and "plant disease control" either together or in combinations.

Statistical Analysis

Using data from each study, two by two tables were prepared and fixed mean differences for plant growth, odd ratios for seed germination and risk ratio for disease control along with their ninety-five percent confidence intervals were calculated by Inverse Variance method using Review Manager 5.4.1 (Rev Man 5.4.1) software. For each indicator, homogeneity was examined by the Breslow-Day test. Further, I^2 -test was used to assess homogeneity using I^2 value of fifty percent as threshold. Forest plots and funnel plots were prepared to visualise data by Rev Man 5.4.1 software.

RESULTS

Study Characteristics

On initial PubMed search, 90 studies were found. After removal of 27 duplicates, 63 studies were reviewed for selection criteria based on title and abstract. Out of these studies, 37 were excluded based on concern of unrelated topics. Remaining 26 studies were reviewed thoroughly for data related to topics of study and 10 studies were removed due to unclear or insufficient data, different language and various other reasons. This left the researchers with 16 studies, which fulfilled selection criteria and were used for systemic review and meta-analysis (Fig.1).

Out of 16 studies included in Table 1, 7 (43.75%) involved the effect of Arsenicum album high dilutions on plants subjected to abiotic stress while 5 (31.25%) belong to use of high dilutions of Gibber-

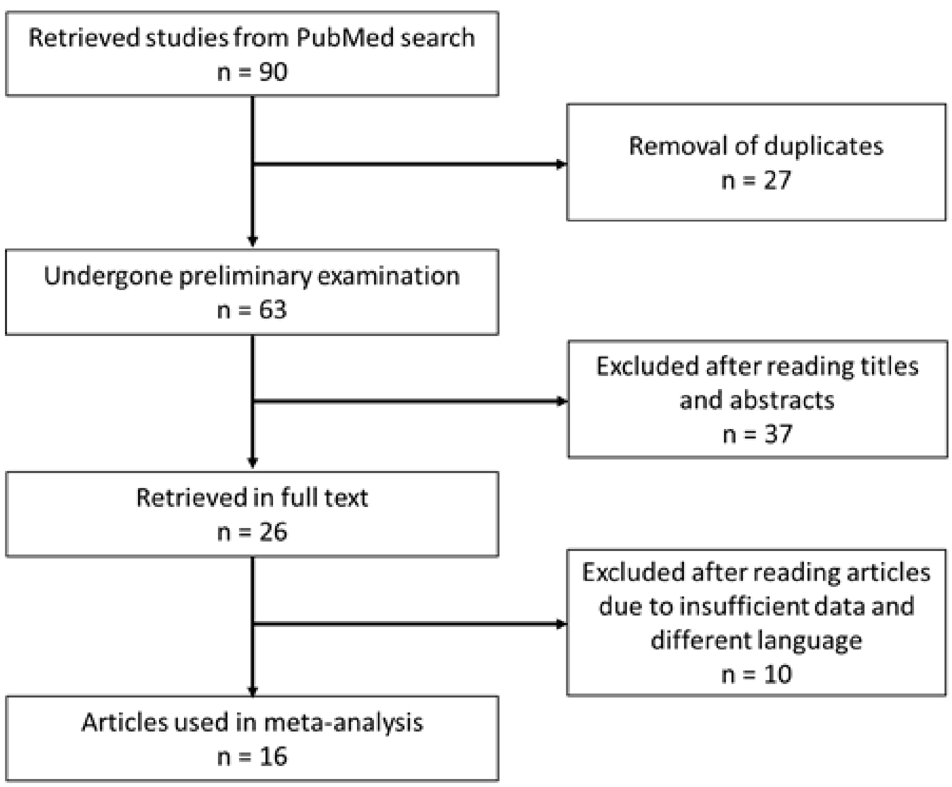

Fig. 1. PRISMA diagram used for meta- analysis

Table 1: Characteristics of studies included in the meta-analysis

Author	*Year*	*Aim*	*Homeopathic agent*	*OutcomeParameter*	*Effects*
Khanna et al. (27)	1977	Effect of four homeopathic drugs on spore germination of *Alternaria alternata*	Kali Iodide, Arsenicum album, *Thuja occidentalis* L.BlattaOrientalis	Percent disease control	Higher doses of Kali Iodide and Arsenicum album were able to control disease significantly
Khanna et al. (6)	1989	Effect of Filix mas and Blatta orientalis on seed mycoflora	*Dryopteris filix-mas* (L.) *Schott*, Blatta Orientalis	Percent occurrence of fungi	Fusarium oxyporum was completely inhibited by both drugs while *Alternaria alternata* was significantly controlled by Blatta orientalis treatment
Khanna et al. (28)	1993	Effect of *Thuja occidentalis* and *Lycopodium clavatum* on *Fusarium* infection	*Thuja occidentalis* L, *Lycopodium clavatum*L	Percent occurrence of fungi	*Fusarium oxyporum* was completely inhibited by both drugs
Betti et al. (19)	1997	Efficacy of Arsenicum album 45x on As_2O_3 exposed seeds	Arsenicumalbum (As_2O_3)	Shoot and root growth	24% higher shoot growth
Brizzi et al. (13)	2000	Effect of Arsenicum album on seed germination	Arsenicumalbum (As_2O_3)	Seed germination	High dilution treatment (30x, 35x,40x, 42x, 45x) increased seed germination
Binder et al. (20)	2005	Effect of Arsenicum album on As_2O_3 exposed seeds	Arsenicumalbum (As_2O_3)	Growth of seedling	Seedling growth reduced
Brizzi et al. (21)	2005	Effect of As_2O_3 in H Don growth of Plants exposed to Sublethaldose of As_2O_3	Arsenicumalbum (As_2O_3)	Seedling length	As_2O_3 45x increased seedling growth
Nani et al. (31)	2007	Efficacy of Arsenicumal bum (45x) on seeds exposed previously to As_2O_3	Arsenicumalbum (As_2O_3)	Seed germination and seedling length	2-12% increase in germination rate and 25% enhancement in seedling growth was observed after treatment.
Lahnstein et al.(30)	2009	Efficacy of ultra high dilutions of Arsenicum album on As_2O_3 exposed seeds	Arsenicumalbum (As_2O_3)	Shoot growth	Reduction of shoot growth
Brizzi et al. (22)	2009	Effects of temperature and aging on the efficacy of As_2O_3 on seed germination	Arsenicumalbum (As_2O_3)	Seed germination	As_2O_3 treatment enhances the germination rate. No change in efficacy of As_2O_3 45× at 20 and 40æ%C while it increases at 70æ%C and decreases at 100æ%C.

Table 1: Contd...

Author	*Year*	*Aim*	*Homeopathic agent*	*Outcome Parameter*	*Effects*
Endler et al. (24)	2011	Efficacy of high dilution ofgibberellic acidon seasonal seedling growth	Gibberellic acid (30x)	Length of seedling	Growth opf seedling was reduced by Gibberellicacid (30x)mainly in autumn.
Pfleger et al. (32)	2011	Effect of high dilution of gibberellic acid on seedling growth	Gibberellic acid (30x)	Seedling length	Gibberellic Acid reduced Seedling growth
Kiefer et al. (29)	2012	Effect of high dilution of gibberellic acidon seed germination	Gibberellic acid (30x)	Seed germination	Gibberellicacid (30x) reduced the germination differentially in different season and year.
Hribar-Marko et al. (26)	2013	Effect of seed pre-treatmentwith gibberellicacid in molecular dose on theefficacy of subsequent gibberellic acid treatmentin high dilution on seedling growth	Gibberellic acid (30x)	Seedling length	Pre-treatment with molecular doses of gibberellic acid induced the inhibitory effect of subsequent treatment of high dilution Gibberellicacid (30x) onseedling growth
Dawar et al. (23)	2015	Antifungal activity of *Thujaoccidentalis* and Natrummuriaticum against *Fusariumoxysporum*	*Thuja occidentalis* L., Natrummuriaticum	Percent colonization	Both treatments reduce the fungal infection
Endler et al. (25)	2015	Effect of high dilution of gibberellic acid on seedling growth in autumn vs. winter-spring	Gibberellic acid (30x)	Stalk length	In all autumn experiments gibberellicacid (30x) reduced seedling growth while the results were inconsistent for winter-spring

ellic acid on healthy plants as the homoeopathic agent. Remaining 4 studies (25%) demonstrated use of various other homoeopathic medicines on phyto-pathological models of wheat plants.

Effect of Treatment of High Dilution of Gibberellic Acid on Healthy Wheat Seeds and Plants

Out of 16, 5 studies exhibited the effect of gibberellic acid on wheat seedlings/stalk growth or wheat seedlings/germination. Further, these studies examined the influence of a homoeopathic high dilution of gibberellic acid at different seasons of the year namely autumn and winter/spring. The researchers performed a season dependent meta-analysis using these studies to examine the effect size and significance level of these studies. The data suggest that treatment with gibberellic acid affects wheat seedlings/stalk growth in a seasonal manner. The forest plot in Table 2 indicates that gibberellic acid reduces the seedlings/stalk growth in autumn with mean difference of -3.99 (95% CI: -4.41, -3.51). The overall effect was found to be significant with P<0.00001. Interestingly, a similar study in the winter/spring season demonstrated a significant increase in seedlings/stalk growth with a mean difference of 1.68 (95% CI: 1.15, 2.21) and P < 0.00001. However, the combined effect of all studies suggests reduction in wheat seedlings/stalk growth upon gibberellic acid treatment as evident by total mean difference of -1.46 (95% CI: -1.82, -1.11) with statistically significant overall effect (P < 0.00001). Further, treatment of gibberellic acid did not show any significant effect on wheat seedlings/germination in both seasons with odd ratios of 1.04 (95% CI: 0.60, 1.80; P = 0.90) and 0.86 (95% CI: 0.40, 1.86; P = 0.70), respectively. The combined overall effect was also statistically insignificant with an odd ratio of 0.97 (95% CI: 0.62, 1.52) and P = 0.90 as evident from Table 3.

Effect of Arsenicum Album High Dilutions on Wheat Plants Subjected to Abiotic Stress

Seven out of 16 studies demonstrated the influence of high dilutions of Arsenicum album on seedlings/stalk growth and seedlings/germination of wheat plants subjected to abiotic stress induced by arsenic. Meta-analysis of these studies depicts that treatment of Arsenicum album significantly

Table 2: Effect of gibberellic acid on wheat seedlings/stalk growth in autumn and winter/spring season

Study or subgroup	*Experimental*			*Control*			*Weight*	*Mean difference IV. Fixed, 95% CI*
	Mean	*SD*	*Total*	*Mean*	*SD*	*Total*		
1.1.1 Autumn Experiment								
Endler 2011	46.97	20.5	4440	50.66	19.8	4440	17.90%	-3.69 [-4.53, -2.85]
Endler 2015	48.3	21.4	5000	52.1	20.4	5000	18.80%	-3.80 [-4.62, -2.98]
Hribar-Marko 2013	60.3	8	500	65.2	7.1	500	14.30%	-4.90 [-5.84, -3.96]
Pfleger 2011	42.5	18.46	1000	45.57	20.3	1000	4.40%	-3.07 [-4.77, -1.37]
Subtotal (95% CI)			**10940**			**10940**	**55.40%**	**-3.99 [-4.47, -3.51]**
Heterogeneity: Chi² = 5.44, df = 3 (P = 0.14); I² = 45%								
Test for overall effect: Z = 16.40 (P < 0.00001)								
1.1.2 Winter/Spring Experiment								
Endler 2011	54.6	16.4	3140	52.68	14.4	3140	21.60%	1.92 [1.16, 2.68]
Endler 2015	54.6	16.4	3000	52.7	14.4	3000	20.70%	1.90 [1.12, 2.68]
Pfleger 2011	38.49	19.39	500	41	18.2	500	2.30%	-2.51 [-4.84, -0.18]
Subtotal (95% CI)			**6640**			**6640**	**44.60%**	**1.68 [1.15, 2.21]**
Heterogeneity: Chi² = 13.10, df = 2 (P = 0.001); I² = 85%								
Test for overall effect: Z = 6.20 (P < 0.00001)								
Total (95% CI)			**17580**			**17580**	**100.00%**	**-1.46 [-1.82, -1.11]**
Heterogeneity: Chi² = 260.86, df = 6 (P < 0.00001); I² = 98%								
Test for overall effect: Z = 8.07 (P < 0.00001)								
Test for subgroup differences: Chi² = 242.32, df = 1 (P < 0.00001), I² = 99.6%								

Source: RevMan 5.4.1

Table 3: Effect of gibberellic acid on wheat seedlings/germination in autumn and winter/spring season

Study or subgroup	*Experimental*		*Control*		*Weight*	*Odds ratio IV, Fixed, 95% CI*
	Events	*Total*	*Events*	*Total*		
2.1.1 Autumn Experiment						
Endler 2011	97	100	96	100	8.70%	1.35 [0.29, 6.18]
Hribar-Marko 2013	99	100	98	100	3.50%	2.02 [0.18, 22.65]
Kiefer 2012	77	100	79	100	45.20%	0.89 [0.46, 1.74]
Pfleger 2011	97	100	96	100	8.70%	1.35 [0.29, 6.18]
Subtotal (95% CI)		**400**		**400**	**66.10%**	**1.04 [0.60, 1.80]**
Total events	370		369			
Heterogeneity: Chi² = 0.72, df = 3 (P = 0.87); I² = 0%						
Test for overall effect: Z = 0.13 (P = 0.90)						
2.1.2 Winter/Spring Experiment						
Endler 2011	95	100	95	100	12.50%	1.00 [0.28, 3.57]
Pfleger 2011	90	100	92	100	21.40%	0.78 [0.30, 2.07]
Subtotal (95% CI)		**200**		**200**	**33.90%**	**0.86 [0.40, 1.86]**
Total events	185		187			
Heterogeneity: Chi² = 0.09, df = 1 (P = 0.76); I² = 0%						
Test for overall effect: Z = 0.39 (P = 0.70)						
Total (95% CI)		**600**		**600**	**100.00%**	**0.97 [0.62, 1.52]**
Total events	555		556			
Heterogeneity: Chi² = 0.96, df = 5 (P = 0.97); I² = 0%						
Test for overall effect: Z = 0.12 (P = 0.90)						
Test for subgroup differences: Chi² = 0.15, df = 1 (P = 0.69), I² = 0%						

Source: RevMan 5.4.1

induces seedlings/stalk growth in wheat seeds previously stressed by arsenic exposure as determined by mean difference of 11.86 (95% CI: 11.67, 12.06). The overall effect was highly significant with $P < 0.00001$ as evident through Table 4.

Further, the forest plot in Table 5 suggests that Arsenicum album treatment enhanced the germination rate of wheat seeds. Higher odds of seed germination were found in the Arsenicum album treated group with an odd ratio of 1.27 (95% CI: 0.87, 1.85). However, the result is debatable as statistical significance was not achieved ($P = 0.22$).

Effect of Homoeopathic Medicine on *Fusarium oxysporum* Infection in Wheat

The researchers further examined the effect of homoeopathic medicine in control of pathogenic fungi *Fusarium oxysporum* in wheat. Two out of 16 studies provided data for five different homoeopathic agents, namely Natrum muriaticum, *Thuja occidentalis* L, Blatta Orientalis, *Dryopteris filix-mas* and *Lycopodium clavatum* L.in controlling infection of *Fusarium oxysporum* in wheat seeds. Data was acquired in the form of percentage occurrence of pathogens and used as a number of events out of 100 in control and treatment groups. The data in Table 6 suggest that all the treatments reduced the risk of *Fusarium* infection in wheat as represented by lower than 1 individual risk ratios and total risk ratio of 0.39 (95% CI: 0.26, 0.60) with overall significant effect ($P < 0.0001$).

Effect of Homoeopathic Medicine on *Alternaria alternate* Infection in Wheat

The researchers studied another phytopathological model of wheat involving *Alternaria alternata* to examine the efficacy of various homoeopathic medicines. Out of 16, two studies reported data related to effect of various homoeopathic medicine, namely Arsenicum album, Kali iodide, *Thuja occidentalis* L., Blatta Orientalis and *Dryopteris filix-mas* in controlling *Alternariaalternata* infection in wheat. Results demonstrate that all treatments showed an inhibitory effect on *Alternaria* infection in wheat, which is evident by individual risk ratio value lower than 1. The total risk ratio was found to be 0.80 (95% CI: 0.75, 0.84). The overall effect was highly significant ($P < 0.00001$) as given in Table 7.

Table 4: Effect of Arsenicum album on wheat seedlings/stalk growth

Study or subgroup	Experimental			Control			Weight	Mean difference
	Mean	*SD*	*Total*	*Mean*	*SD*	*Total*		*IV. Fixed, 95% CI*
Binder 2005	50.6	10.94	1098	52	9.95	1109	5.00%	-1.40 [-2.27, -0.53]
Brizzi 2005	75.1	2.57	30	72.2	3.07	30	1.90%	2.90 [1.47, 4.33]
Lahnstein 2009	44.1	11.35	845	45.8	10.95	853	3.40%	-1.70 [-2.76, -0.64]
Nani 2007	75.1	0.47	33	61.8	0.38	33	89.70%	13.30 [13.09, 13.51]
Total (95% CI)			**2006**			**2025**	**100.00%**	**11.86 [11.67, 12.06]**

Heterogeneity: $Chi^2 = 1851.88$, df = 3 ($P < 0.00001$); $I^2 = 100\%$
Test for overall effect: $Z = 119.01$ ($P < 0.00001$)

Source: RevMan 5.4.1

DISCUSSION

Many critics regularly argue about the lack of scientific basis and theoretical models in homoeopathy. Hence, well defined research models are the need of time for homoeopathy. However, various methodological hindrances and lower research investment restrict homoeopathy researchers from fulfilling this goal. Plant and microorganism-based experimentation models may be suitable candidates for this goal, as botanical and microbial trials do not concern the placebo effect and ethical problems and provide low cost and almost unlimited amounts of biological materials (Betti et al. 2008; Baumgartner et al. 1998). Further, it can generate essential data for use of homoeopathy in plant growth and disease management. However, till now only limited research has been performed in this area. Further, un-reproducibility of results makes this problem bigger. Performing meta-analysis of previously conducted studies, which may provide crucial information about effect size and significance of result, may further be used to select and design studies with effective homoeopathic medicines for plant growth and control of phyto-pathogen and pests.

Here in the researchers' best knowledge, for the first time they have performed a meta-analysis on the effect of various homoeopathic medicines on plant growth and disease management in wheat. They chose wheat for this study, as it has been reported as the most often used species in homoeopathic studies on plant models (Teixeira et al. 2017). In the current study, the researchers have discussed the effect of homoeopathic agents on germination and growth of healthy and abiotically stressed wheat seedling/plants and control of disease in phyto-pathogenic models.

The researchers examined 16 studies, among which 5 were related to the effect of gibberellic acid treatment on wheat seedling/germination and stalk growth in a seasonal manner. Previously, studies have reported that treatment with gibberellic acid 30X reduces the wheat seedling growth more prominently in the autumn season, while results in winter/spring season were inconsistent (Endler et al. 2015; Endler et al. 2011). Hribar-Marko et al. (2013) tested the hypothesis that pre-treatment of grains with gibberelic acid at high concentrations inhibits stalk growth during autumn. They had to reject this hypothesis due to lack of significant

Table 5: Effect of Arsenicum album on wheat seedlings/germination

Study or subgroup	Experimental		Control		Weight	Odds ratio IV, Fixed, 95% CI
	Events	Total	Events	Total		
Brizzi 2000	87	100	87	100	21.20%	1.00 [0.44, 2.28]
Brizzi 2009	90	100	83	100	20.60%	1.84 [0.80, 4.25]
Lahnstein 2009	75	100	75	100	35.10%	1.00 [0.53, 1.90]
Nani 2007	88	100	82	100	23.10%	1.61 [0.73, 3.55]
Total (95% CI)		**400**		**400**	**100.00%**	**1.27 [0.87, 1.85]**
Total events	340		327			
Heterogeneity: $Chi^2 = 1.97$, df = 3 (P = 0.58); $I^2 = 0\%$						
Test for overall effect: Z = 1.22 (P = 0.22)						

Source: RevMan 5.4.1

Table 6: Effect of homeopathic medicines on fusarium infection in wheat

Study or subgroup	Experimental		Control		Weight	Odds ratio IV, Fixed, 95% CI
	Events	Total	Events	Total		
Dawar 2015 (Natrum Muriaticum)	10	100	25	100	39.00%	0.33 [0.15, 0.74]
Dawar 2015 (Thuja Occidentalis)	15	100	25	100	48.70%	0.53 [0.26, 1.08]
Khanna 1989 (Blatta Orientalis)	0	100	14	100	3.10%	0.03 [0.00, 0.50]
Khanna 1989 (Filix Mas)	0	100	14	100	3.10%	0.03 [0.00, 0.50]
Khanna 1993 (Lycopodium Clavatum)	0	100	20	100	3.10%	0.02 [0.00, 0.33]
Khanna 1993 (Thuja Occidentalis)	0	100	20	100	3.10%	0.02 [0.00, 0.33]
Total (95% CI)		**600**		**600**	**100.00%**	**0.30 [0.18, 0.50]**
Total events	25		118			
Heterogeneity: $Chi^2 = 14.84$, df = 5 (P = 0.01); $I^2 = 66\%$						
Test for overall effect: Z = 4.73 (P < 0.00001)						

Source: RevMan 5.4.1

Table 7: Effect of homeopathic medicines on fusarium infection in wheat

Study or subgroup	Experimental		Control		Weight	Odds ratio IV, Fixed, 95% CI
	Events	Total	Events	Total		
Khanna 1977 (Arsemicum Album)	58	100	100	100	2.70%	0.01 [0.00, 0.11]
Khanna 1977 (Kali Iodide)	41	100	100	100	2.70%	0.00 [0.00, 0.06]
Khanna 1977 (Thuja Occidentalis)	91	100	100	100	2.60%	0.05 [0.00, 0.83]
Khanna 1989 (Blatta Orientalis)	8	100	66	100	30.60%	0.04 [0.02, 0.10]
Khanna 1989 (Filix Mas)	33	100	66	100	61.40%	0.25 [0.14, 0.46]
Total (95% CI)		**500**		**500**	**100.00%**	**0.12 [0.07, 0.18]**
Total events	231		432			
Heterogeneity: $Chi^2 = 22.12$, df = 4 (P = 0.0002); $I^2 = 82\%$						
Test for overall effect: Z = 9.19 (P < 0.00001)						

Source: RevMan 5.4.1

difference in stalk growth. In another study, Kiefer et al. (2012) reported 2 sets of experiments (4 each), first between 2009-2010 and second in 2011where gibberellic acid 30X significantly lowered the germination rate in wheat by 4.4 percent as compared to the control group. Hence, in this study the researchers selected data only related to gibberellic acid 30X. They also found similar results where a highly significant inhibitory effect on wheat seedling/stalk growth was observed after gibberellic acid treatment in autumn while the contradictory effects were observed in 3 included studies performed in winter/spring season with overall inducing effect. However, a total combined effect of autumn and winter/spring studies suggested inhibitory potential of gibberellic acid on wheat seedling/stalk growth. However, they did not find a statistically significant effect on seedling/germination after treatment with gibberellic acid 30X in both seasons. Pfleger et al. (2011) also studied the effect of gibberellic acid 30X on growth of the wheat stalk. In this study, through the results obtained, it was evident that stalk length after treatment with gibberellic acid 30X was 8.35 percent smaller than the control stalk length. Although, studies included in the meta-analysis have reported higher germination rate in autumn in response to gibberellic acid but their statistical significance is arguable. Further, associated data germination rate in winter/spring season was inconsistent and the overall effect was also insignificant. This suggests that seedling/germination may not be an ideal parameter to assess the effect of gibberellic acid on wheat plant growth.

Effect of Arsenicum Album Treatment on Seedling/Germination and Shoot/Stalk Growth on Wheat Seeds

7 out of 16 studies discussed the effect of Arsenicum album treatment on seedling/germination and shoot/stalk growth on wheat seeds previously stressed by arsenic. Reports have suggested the positive role of high dilutions of homoeopathically potentised Arsenicum album in seedling/germination and growth in various plant species in non-stressed as well as stressed conditions. Brizzi et al. (2000) reported that use of 45X dilution of Arsenicum album was able to induce germination in healthy wheat seeds.Whereas, Binder et al.(2005) reported that Arsenicum Album 45X inhibited wheat shoot growth compared to control group (unpotentized water) instead of enhancing it. Lahnstein et al. (2009) reported 2 studies where significant increase in shoot growth after treatment with Arsenicum Album 45x in those plants which were prior toxicated with Arsenic Trioxide. Whereas in another study, the shoot growth was retarded after treatment with Arsenicum Album 45x. No significant results in shoot length were observed in newly performed experiments. Further, Jäger et al. (2011) demonstrated that treatment of abiotically stressed *Lemna gibba* species with potentiated Arsenicum album and nosode promote plant growth (Teixeira et al. 2017). Moreover, various studies in abiotically stressed wheat models exhibited similar results (Brizzi et al. 2009; Nani et al. 2007; Baumgartner et al. 2004; Betti et al. 1997). In the meta-analysis, the researchers included all relevant data associated with the effect of 45X dilution of homoeopathically potentised Arsenicum album on seedling germination and growth of abiotically stressed wheat. Results suggested that Arsenicum album could not enhance seed germination rate in wheat. Although the data demonstrated slightly higher odds of seed germination in the treatment group as compared to control, the overall effect was statistically insignificant. However, Arsenicum album treatment significantly elevated the abiotically stressed wheat seedling/shoot growth. Despite studies involved in meta-analysis of seedling/shoot growth data showing inconsistent or contradictory results, the overall effect showed significantly higher mean difference in seedling/shoot sizes of treated versus control groups. These observations indicate that high dilution of Arsenicum album may be used to stimulate the growth of wheat seedlings, which have undergone abiotic stress. However, it may not be applicable to seed germination.

Homoeopathic Management of *Fusarium oxysporum* and *Alternaria alternate* Infection in Wheat

Further, four out of 16 studies dealt with therapeutic effects of various homoeopathic agents in the management of *Fusarium oxysporum* and *Alternaria alternata* infection in wheat. Khanna et al. (1989) demonstrated that treatment with various homoeopathic potencies of *Dryopteris filix-mas* and Blatta Orientalis induced qualitative and quantitative variations in mycoflora of wheat seeds. The result revealed that *Fusarium oxysporum* and *Alternaria alternata* were the dominant fungi in untreated seeds and were significantly suppressed by 30 and 200 potencies of *Dryopteris filix-mas* and Blatta Orientalis. Similarly, few other reports have indicated the inhibitory effects of various homoeopathic agents against the infection of these fungi species (Dawar et al. 2015; Khanna 1993; Khanna and Chandra1977). Hence, the researchers performed meta-analysis on the effect of homoeopathy in wheat plant disease control using *Fusarium oxysporum* and *Alternaria alternata* as phytopathogenic models.

Here, the researchers examined the data associated with effect of Natrum muriaticum 200, *Thuja occidentalis* 30 and 200, Blatta orientalis 200, Filix mas 200 and *Lycopodium clavatum* 200 on occurrence of *Fusarium oxysporum* in wheat seeds. The results showed that all the homoeopathic agents could highly reduce the risk of *Fusarium* infection individually. Further, overall results also indicate towards significantly lower risk ratios. Similarly, Arsenicum album 200, Kali iodide 200, Thuja occidentalis 30, Blatta orientalis 200 and Filix mas 200 could individually inhibit the risk of *Alternaria alternata* infection in wheat and with significant overall effect. These observations contribute vital information, which can be translated in use of these homoeopathic agents as therapeutic candidates for control of *Fusarium* and *Alternaria* infection in wheat. It may also be a template for conducting further experiments involving use of these homoeopathic agents either alone or in combination to control the infection of pathogenic mycoflora in various plants including wheat.

LIMITATIONS

The researchers acknowledge certain limitations of the study. Primarily, the use of studies published only in English language led to missing out some interesting data, which could have been beneficial to consolidate the findings of this meta-analysis. Further, the researchers have used the data associated with homoeopathic potencies with highest effect only and did not consider many other potencies with lower effect as reported in included studies. However, using all data related to all the reported potencies may have made conducting this meta-analysis very complicated and complex to understand. Arguably, the effect of more homoeopathic agents may have been studied but lack of sufficient studies and relevant data did not allow for that. Overall, the study demonstrated a high degree of heterogeneity as evident by P and I^2 values in heterogeneity analysis except seed germination data. The seed germination data was reported in the form of percent seed germination in most of the studies so the researcher represented it as a number of events out of 100. This led to absence of heterogeneity in study populations.

CONCLUSION

In conclusion, this study provides useful insight for use of various homoeopathic medicines for seed germination and growth in wheat. It suggests that use of homoeopathically potentised gibberellic acid significantly reduces the wheat seedling/stalk growth in autumn season with no or inconclusive effect in winter/spring season. There was no conclusive effect on seed germination also. Further, Arsenicum album treatment was found to increase the growth of seedling/shoot in abiotically stressed wheat while there was no significant effect on seed germination rate. Moreover, various homoeopathic agents showed significant effects in reducing risk of *Fusarium* and *Alternaria* infection in wheat plants.

RECOMMENDATIONS

Overall, the crucial information generated from this study may be used to design further translational studies for the use of homoeopathic agents in plant growth and disease management targeting specific plant infestation.

This may lead to formulation of plant based herbal products as replacement for pesticides and eventually leading to establishment of a start-up in the field of agro-homeopathy.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

FUNDING

The authors have received no funding for this manuscript.

INFORMED CONSENT

Not applicable

ETHICAL APPROVAL

Not applicable.

ACKNOWLEDGMENTS

The authors would like to thank the Honourable Chancellor of Dr. D.Y. Patil Vidyapeeth, Pune, Dr. P.D. Patil for giving them the opportunity to write this meta-analysis. Authors would also like to thank the Vice Chancellor of Dr. D.Y. Patil Vidyapeeth, Pune, Professor Dr. N. J. Pawar for his constant support and guidance. The authors would like to thank the Honourable Trustee of Dr. D.Y. Patil Vidyapeeth, Dr.Smita Jadhav for her constant source of inspiration. The authors would also like to thank Dr. Ramesh Bhonde, Director, Research, Dr. D.Y. Patil Vidyapeeth, Pune for his constant support and expertise. Last but not the least, the researchers would like to thank Dr. Indumathi Somasundaram, Proprietor, Indu's Academy of Biology and Medicine and her team for logistical and technical support.

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Paper received for publication in May, 2022
Paper accepted for publication in May, 2023