

ORIGINAL ARTICLE

Dermal Risk Assessment of Glyphosate Exposure at Agricultural Field-Use Concentrations

Siti Zulaikha Rusmadi¹, Sharifah Norkhadijah Syed Ismail¹, Manraj Singh Cheema², Vivien How¹

¹ Department of Environmental and Occupational Health, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, 43400 Serdang, Selangor, Malaysia

² Department of Biomedical Sciences, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, 43400 Serdang, Selangor, Malaysia

ABSTRACT

Introduction: Dermal exposure is the primary concern for glyphosate exposure, particularly in occupational setting mainly due to the nature of the work with varying degrees of pesticide. This study evaluates the potential dermal health risks associated with exposure to glyphosate at concentrations commonly used in agricultural settings, at 1–2%. **Method:** A quantitative risk assessment was conducted using the Hazard Quotient (HQ) approach, where HQ is defined as the ratio of the estimated average daily dose (ADD) to the established Reference Dose (RfD). The absorbed dose was calculated by incorporating key parameters such as chemical concentration, skin permeability, contact time, and exposed skin surface area. **Results:** This study models the risk for males at average body weight of 80.2 kg and exposed skin area of 4210 cm² and females at average body weight of 67.3 kg and exposed skin area of 3260 cm². With the exposure to glyphosate concentrations between 0.0001% and 3.5%, the calculated HQ for male was ranged from 7.5×10^{-8} to 2.65×10^{-3} and from 7.0×10^{-8} to 2.45×10^{-3} for female. All HQ values remained well below the threshold of 1, indicating low likelihood of adverse health effects under the assessed exposure scenario. However, it should be noted that the permeability coefficient (K_p) used in this assessment was based on glyphosate alone, not on commercial formulations. **Conclusion:** These findings highlight the need for continued adherence to PPE usage as a precautionary measure especially when the extent of dermal absorption with the presence of adjuvants remains underreported.

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Corresponding Author:

Sharifah Norkhadijah Syed Ismail, PhD

Email: norkhadijah@upm.edu.my

Tel: +60397692395

Fax: +60397692395

INTRODUCTION

Glyphosate-based herbicides (GBHs) are the most widely used broad-spectrum, non-selective herbicides globally, with glyphosate serving as the active ingredient [1, 2]. In Malaysia, it is the most used herbicide accounting for 70% of the country total pesticide consumption [3, 4]. Approximately, 15 million litters are sold annually in Malaysia [5, 6].

Glyphosate was first authorised as an herbicide in 1974 in the U.S. following Environmental Protection Agency (EPA) approval for its use [7, 8]. It underwent several renewal and re-evaluation processes by EPA as well as other international regulatory bodies after the initial

authorisation and consistently identified as no concern for human health [9]. In 2015, International Agency for Research on Cancer (IARC) classified glyphosate and its derivatives as probable human carcinogens (Group 2A). Following this, regulatory authorities re-evaluated glyphosate carcinogenic potential. In 2016, following comprehensive reviews of epidemiological, animal, and genotoxicity data, it is concluded that glyphosate is unlikely to pose a carcinogenic risk to humans [10, 11]. Despite the potential health risks concluded from various regulatory bodies, concerns remain regarding occupational exposure, particularly through dermal contact. Dermal exposure is a significant route of glyphosate exposure for agricultural workers during mixing, loading, and application activities [12]. Studies have detected glyphosate in the urine of farmers around the application periods indicating systemic absorption occurs primarily through skin contact [13]. More recent study in Iowa and North Carolina also echoing the same sentiment in which glyphosate detected in urine of farmers primarily reflects recent exposure and that

dermal contact is the predominant route occupationally [14]. Dermal penetration experiments indicated that the percutaneous absorption of glyphosate was less than 2% when left undisturbed on the skin surfaces of experimental animals and on human skin in vitro [13].

Commercial GBH are composed of glyphosate as the active ingredient and adjuvant as inert ingredient added into the formulation to improve herbicidal effectiveness [15, 16]. A growing body of in vitro research consistently demonstrate that GBHs, which include active ingredient and adjuvants, are significantly more toxic than glyphosate alone. Gasnier et al. showed that various GBHs provoked liver cell death in HepG2 and Hep3B cells, with greater effects attributed to the presence of adjuvants [17]. Similarly, Koller et al. found that GBH exposure caused strong cytotoxic responses in buccal epithelial cells exceeding the effects of glyphosate alone [18]. While glyphosate by itself often required high concentrations to caused measurable cytotoxic effects, its formulations consistently caused more severe responses even at lower doses [19, 20].

Given the widespread use of GBHs and their potential for dermal exposure, there is a clear need to assess the associated health risks under realistic occupational exposure conditions to the agriculture workers. While glyphosate is generally considered to have low dermal toxicity, questions remain regarding its safety at concentrations commonly used in the field. Furthermore, commercial formulations of GBHs often contain adjuvants that increase their overall cytotoxicity, which may also contribute to enhanced dermal toxicity [21].

Despite extensive research on glyphosate toxicity, and occupational exposure, most studies focused on in vitro toxicity or biomonitoring data, with limited application of the Hazard Quotient (HQ) approach to evaluate dermal exposure under realistic agricultural conditions. While GBH dominate pesticide use, limited studies have incorporated usage patterns as well as gender specific exposure assessment. Therefore, this study aims to evaluate the potential dermal health risks of glyphosate exposure by conducting a quantitative risk assessment using the HQ approach. It will integrate the exposure models, toxicological reference values, and realistic agricultural-use concentrations to determine risk estimate for both male and female agricultural workers.

MATERIALS AND METHODS

Study Design

This study employed a scenario-based quantitative risk assessment to model potential human health associated with glyphosate exposure at field-use concentrations. The assessment focused primarily on agricultural workers. However, no human participants were recruited, and no primary field measurements or biological samples were collected at any stage of the

study. Instead, all data inputs were derived from existing field measurements, regulatory reports, and established toxicological databases reported in the literature.

The modelling approach integrates exposure parameters (glyphosate concentration, dermal permeability, contact duration, and skin surface area) with toxicological reference values to estimate absorbed doses and hazard quotients under realistic occupational scenarios. This assessment assumes that exposure occurs exclusively through dermal contact, dermal absorption is uniform across all exposed skin areas, and the skin surface area values represent the maximum exposed area during glyphosate handling and application.

Risk Assessment

Risk assessment was conducted specifically for agricultural workers, who are directly involved in the preparation, handling, and application of glyphosate in the field and was quantitatively focused on dermal exposure. The assessment followed the basic framework for carrying out health risk assessments established by the National Research Council (NRC) in 1983 [22]. It is a four-step framework used in human health risk evaluations that includes hazard identification, dose-response assessment, exposure assessment, and risk characterization. **Fig. 1** show the flow diagram of the risk assessment steps [22].

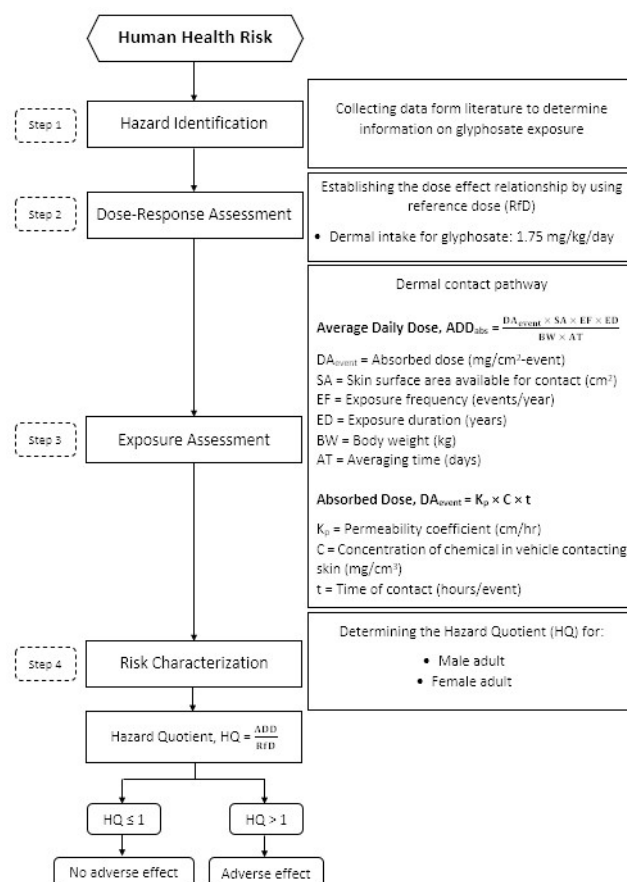


Fig. 1: Flow diagram of the risk assessment step

I. Hazard Identification

While glyphosate is generally considered to have low acute dermal toxicity, repeated or chronic exposure particularly through commercial formulations containing adjuvants may alter absorption potential [2, 12]. Information on glyphosate concentration used in field was gathered from various literatures.

II. Dose-Response Assessment

The Reference Dose (RfD) of 1.75 mg/kg/day used in this study is based on the oral RfD for glyphosate, as a dermal RfD is not available due to glyphosate's low dermal absorption [23]. This value was used as a surrogate benchmark for toxicity. RfD allows for the establishment of a dose-effect relationship.

III. Exposure Assessment

The estimated dermal exposure was calculated in a step-by-step manner. The absorbed dose was first calculated as shown below in Equation 1 [24]:

$$\text{Absorbed Dose, } DA_{\text{event}} = K_p \times C \times t \quad (1)$$

Where:

K_p = Permeability coefficient (cm/hr)

C = Concentration of chemical in vehicle contacting skin (mg/cm³)

t = Time of contact (hours/event)

The absorbed dose per event (DA_{event}) represents the amount of glyphosate absorbed through the skin when the substance is present as a liquid or aqueous mixture. In the next step, the average daily dose (ADD) was calculated following the determination of DA_{event} values, as shown in Equation 2:

$$\text{Average Daily Dose, } ADD_{\text{abs}} = (DA_{\text{event}} \times SA \times EF \times ED) / (BW \times AT) \quad (2)$$

Where:

DA_{event} = Absorbed dose (mg/cm²-event)

SA = Skin surface area available for contact (cm²)

EF = Exposure frequency (events/year)

ED = Exposure duration (years)

BW = Body weight (kg)

AT = Averaging time (days)

IV. Risk Characterization

The hazard quotient (HQ) was calculated separately for males and females across various glyphosate concentrations. HQ was calculated as the following Equation 3:

$$\text{Hazard Quotient, } HQ = ADD/RfD \quad (3)$$

All HQ values were interpreted relative to the risk threshold of 1. HQ values below this threshold indicate that under the modelled scenarios, dermal exposure to glyphosate is not expected to pose significant health

risks [25].

Table I list all the parameters included in the determination of absorbed dose, average daily intake and hazard quotient through dermal exposure. Glyphosate concentrations ranged was based on the typical agricultural use concentration of glyphosate, which falls between 1% and 3%, reflecting typical agricultural used formulations [19, 26-28]. The permeability coefficient (K_p) of 5.9×10^{-6} cm/h was based on pure glyphosate, not commercial mixtures. This is the most recent permeability coefficient published for glyphosate [29]. Time of contact (h) per events were extracted from various studies, where selected exposure duration aligns with common occupational exposure times to pesticides, which typically range between 30 minutes and 7 hours during agricultural or pesticide-related tasks. However, this duration was extended up to 24 hours to see possible variation of risk potential [30-34]. The skin surface area available for contact (SA) for male was 4210 cm², and for female 3260 cm² [35]. These values were obtained from United States Environmental Protection Agency (USEPA), Exposure Factors Handbook for the arms and hands, which are the body parts most exposed during pesticide-related work. Differentiating the risk assessment between male and female was done because dermal exposure is directly proportional to the skin surface area available for contact, in this case, males have a larger skin surface area than females [35].

Table I: Parameter Values for Human Health Risk Assessment

Parameter	Value	Reference
K_p = Permeability coefficient (cm/hr) for glyphosate	0.0000059 cm/h, 5.9×10^{-6} cm/h	[29]
C = Concentration of chemical in vehicle contacting skin (mg/cm ³)	0.001, 0.01, 0.1, 1, 2, 5, 10, 15, 20, 25, 30, 35 mg/cm ³ Concentration of glyphosate and its formulation for this study in %, therefore, it is was converted to mg/cm ³ prior calculation for health risk assessment.	[27, 28]
t = Time of contact (hours/event)	0.5, 1, 4, 6, 9, 12, 15, 18, 24 h	[30-34]
SA = Skin surface area available for contact (cm ²)	Arm and hands: Male (4210 cm ²) Female (3260 cm ²)	[35]
EF = Exposure frequency (events/year)	17.07 events/year	[36]
ED = Exposure duration (years)	16.47 years	[36]
BW = Body weight (kg)	Male 80.2kg Female 67.3kg	[35]
AT = Averaging time (days)	6011.55	[35]
RfD = Reference dose	1.75 mg/kg/day	[37]

RESULTS

The HQ values were calculated for both male and female agricultural workers across a range of glyphosate concentrations (0.0001% to 3.5%). **Table II** summarizes the corresponding HQ values under different exposure scenarios.

For males (body weight: 80.2 kg; exposed skin area: 4210 cm²), HQ values ranged from 7.5×10^{-8} to 2.65×10^{-3} . For females (body weight: 67.3 kg; exposed skin area: 3260 cm²), HQ values ranged from 7.0×10^{-8} to 2.45×10^{-3} . In all modelled cases, HQ values remained well below the threshold of 1, indicating low likelihood of adverse health effects under the assessed exposure scenario. In addition, HQ values assessed in this study does not account for mixture effects, adjuvant toxicity, or chronic outcomes.

The HQ values increased with glyphosate concentration, however, even at highest concentration of 3.5%, the HQ did not exceed 1 for either gender, reinforcing the low risk across all tested exposure levels.

DISCUSSION

The results of this quantitative risk assessment suggest that dermal exposure to glyphosate at agricultural field-use concentrations is unlikely to pose significant health risks to agricultural workers under typical exposure scenarios. The Hazard Quotient (HQ) values in this study remained

well below the regulatory threshold of 1, indicating that the estimated absorbed doses fall within acceptable safety levels. This aligns with previous research, which shows that glyphosate exhibits low dermal toxicity in its pure form [38]. Additionally, studies focusing on occupational exposure have similarly concluded that glyphosate exposure remains below safety thresholds for agricultural workers [39].

Although estimated risks are low, these findings support maintaining basic safety practices, such as minimizing direct skin contact and following proper hygiene, to account for variability in exposure as well as the potential influence of inert ingredient presence in commercial formulation. The slightly higher HQ values observed in males can be attributed to factors such as larger skin surface area and higher body weight. However, these physiological differences do not alter the overall risk classification.

Risk assessments of glyphosate exposure via ingestion have also yielded reassuring results. For instance, studies on glyphosate ingestion through water consumption show HQ values of less than 1 across all population groups, suggesting no significant health risks [40]. Furthermore, internal dose estimates based on urinary glyphosate concentrations, used as a biomarker of overall exposure, also support these findings. Specifically, sprayers demonstrated the HQ value for glyphosate exposure of less than 1, indicating that systemic exposure, assessed from biomarker data, remains within the safe range [36].

Table II: Hazard Quotient (HQ) values with respect to different gender

Gender	BW	SA	Concentration (mg/cm ²)	Hazard Quotient (HQ)		Gender	BW	SA	Concentration (mg/cm ²)	Hazard Quotient (HQ)	
				AVG±SD	Range					AVG±SD	Range
Male	80.2 kg	4210 cm ²	0.001	0.0075x10 ⁻⁵ ± 0.0066x10 ⁻⁵	0.0004x10 ⁻⁵ – 0.02x10 ⁻⁵	Fe-male	67.3 kg	3260 cm ²	0.001	0.0070x10 ⁻⁵ ± 0.0061x10 ⁻⁵	0.0003x10 ⁻⁵ – 0.02x10 ⁻⁵
			0.01	0.08x10 ⁻⁵ ± 0.07x10 ⁻⁵	0.0041x10 ⁻⁵ – 0.20x10 ⁻⁵				0.01	0.07x10 ⁻⁵ ± 0.06x10 ⁻⁵	0.0038x10 ⁻⁵ – 0.18x10 ⁻⁵
			1	7.57x10 ⁻⁵ ± 6.59x10 ⁻⁵	0.41x10 ⁻⁵ – 19.86x10 ⁻⁵				1	6.99x10 ⁻⁵ ± 6.08x10 ⁻⁵	0.38x10 ⁻⁵ – 18.33x10 ⁻⁵
			2	15.15x10 ⁻⁵ ± 13.17x10 ⁻⁵	0.83x10 ⁻⁵ – 39.73x10 ⁻⁵				2	13.98x10 ⁻⁵ ± 12.16x10 ⁻⁵	0.76x10 ⁻⁵ – 36.66x10 ⁻⁵
			5	37.87x10 ⁻⁵ ± 32.94x10 ⁻⁵	2.07x10 ⁻⁵ – 99.32x10 ⁻⁵				5	34.94x10 ⁻⁵ ± 30.39x10 ⁻⁵	1.91x10 ⁻⁵ – 91.65x10 ⁻⁵
			10	75.7x10 ⁻⁵ ± 65.87x10 ⁻⁵	4.14x10 ⁻⁵ – 198.64x10 ⁻⁵				10	69.88x10 ⁻⁵ ± 60.78x10 ⁻⁵	3.82x10 ⁻⁵ – 183.30x10 ⁻⁵
			15	113.60x10 ⁻⁵ ± 98.81x10 ⁻⁵	6.21x10 ⁻⁵ – 297.96x10 ⁻⁵				15	104.83x10 ⁻⁵ ± 91.17x10 ⁻⁵	5.73x10 ⁻⁵ – 274.95x10 ⁻⁵
			20	151.47x10 ⁻⁵ ± 131.74x10 ⁻⁵	8.28x10 ⁻⁵ – 397.29x10 ⁻⁵				20	139.77x10 ⁻⁵ ± 121.57x10 ⁻⁵	7.64x10 ⁻⁵ – 366.61x10 ⁻⁵
			25	189.33x10 ⁻⁵ ± 164.68x10 ⁻⁵	10.34x10 ⁻⁵ – 496.61x10 ⁻⁵				25	174.71x10 ⁻⁵ ± 151.96x10 ⁻⁵	9.55x10 ⁻⁵ – 458.26x10 ⁻⁵
			30	227.20x10 ⁻⁵ ± 197.61x10 ⁻⁵	12.42x10 ⁻⁵ – 595.93x10 ⁻⁵				30	209.65x10 ⁻⁵ ± 182.35x10 ⁻⁵	11.46x10 ⁻⁵ – 549.91x10 ⁻⁵
			35	265.06x10 ⁻⁵ ± 230.55x10 ⁻⁵	14.48x10 ⁻⁵ – 695.25x10 ⁻⁵				35	244.59x10 ⁻⁵ ± 212.74x10 ⁻⁵	13.37x10 ⁻⁵ – 641.56x10 ⁻⁵

When compared to other pesticides, similar risk assessments have demonstrated acceptable levels of exposure. For instance, Siriwat et al. assessed the health risks of skin exposure to chlorpyrifos among children in agricultural areas of Sakon Nakhon Province, Thailand. Their study found the HQ for child dermal exposure to chlorpyrifos to be 0.03, indicating a low risk well within the acceptable safety margin [41]. Similarly, Chidya et al. conducted a risk assessment for pesticides in the Kurose River and its catchment area in Japan. Their assessment found that all the pesticides evaluated, including cyanazine, simetryn, and diazinon, had HQ values below the regulatory threshold of 1, posing no significant health risks to humans [42]. These comparative assessments supporting the reliability of the current dermal risk estimates for glyphosate by demonstrating consistent HQ values below regulatory thresholds across different pesticides and exposure scenarios.

It is important to note that the HQ values reflect only short-term exposure and do not account potential long-term glyphosate exposure. Long-term in vivo studies indicate that exposure to GBH may result in cumulative physiological changes, including decreased antioxidant enzyme activity, alterations in gut microbiota, and reproductive hormone disruption [43]. Moreover, there are concerns regarding neuroendocrine effects and potential neurotoxicity [44]. Such findings suggest that traditional HQ assessments based on short-term toxicity may not fully capture the subtle, chronic effects of long-term exposure. However, it is important to exercise caution despite the apparent safety of short-term dermal exposure.

Study Limitation

One limitation of this study is that the risk assessment used a permeability coefficient (K_p) based solely on glyphosate, therefore excluding the effects of adjuvants commonly found in commercial GBH. These adjuvants are known to enhance toxicity, potentially elevating the risk [19]. Furthermore, the assessment assumed homogeneous exposure across the entire skin surface, did not model chronic or repeated exposures. These simplifications may underestimate real-world dermal absorption and long-term risk. Factors such as skin damage, repeated or chronic exposures, and potential synergistic interactions could also increase the overall risk following exposures. This study focuses on specific occupational group which is agricultural workers as they represent the highest dermal exposure group among direct handlers and applicators. The workers exposed to repeated field-use concentrations and prolonged contact condition. Extrapolation of the dermal glyphosate exposure findings to other occupational settings should be undertaken cautiously due to differences in exposure intensity, application methods, environmental conditions, and protective practices. In the context of when no human is directly present, exposure risk does

not disappear. For example, the risk may be generated from mechanised or automated spraying such as drone or during post-application phase after workers leave field. Human dermal exposure may be minimal, but the maintenance workers, equipment cleaners and field re-entry workers may still face the exposure.

CONCLUSION

In conclusion, the results of this risk assessment following dermal exposure to glyphosate at concentrations commonly used in agricultural settings (1–2%) suggest is generally below established toxicological threshold levels. The HQ value of less than 1 for each gender suggests a low likelihood of adverse health effects under the assessed conditions. However, there is limitations presence in short-term HQ models, including the use of a glyphosate skin permeability coefficient alone and the exclusion of adjuvant effects, highlight the need for more comprehensive evaluations. Future study also may consider the task-based exposure assessment instead of focusing only on job category to break down the exposure by specific tasks such as mixing/loading, spraying, equipment cleaning etc. This will improve the precision in dermal exposure estimation by identifying the highest-risk activities and suggest targeted risk mitigation strategies. To address the “no direct human involvement”, a scenario-based exposure modelling can be applied such as through sensitivity analysis, Monte Carlo simulation or worst-case vs realistic exposure comparison. This allows broader applicability of the results, and the risk can be projected across occupational categories and reduce uncertainty.

Although the findings suggest a low dermal risk for agricultural workers, continued use of personal protective equipment (PPE) and strict adherence to safe handling practices remain essential. Given that dermal exposure is not the primary exposure route for non-agricultural populations, the low potential health risk observed for agricultural workers may also indicate a low likelihood of adverse health effects for surrounding communities under normal agricultural practices. Future research should focus on evaluating dermal long-term effects of commercial formulations containing adjuvants and consider chronic or repeated exposures to better inform occupational safety guidelines.

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