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A mechanistic kinetic model for lipid oxidation in Tween 20-stabilized O/W emulsions

Khoa A. Nguyen^a, Vincent J.P. Boerkamp^a, John P.M. van Duynhoven^{b,c}, Arend Dubbelboer^d, Marie Hennebelle^{a,*}, Peter A. Wierenga^a

^a Wageningen University & Research, Laboratory of Food Chemistry, Bornse Weilanden 9, 6708 WG Wageningen, the Netherlands.

^b Unilever Food Innovation Centre, Bronland 14, 6708 WH Wageningen, the Netherlands.

^c Wageningen University & Research, Laboratory of Biophysics, Stippeneng 4, 6708 WE, Wageningen, the Netherlands.

^d Danone Nutricia Research, Uppsalalaan 12, 3584 CT Utrecht, the Netherlands

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ABSTRACT

Models predicting lipid oxidation in oil-in-water (O/W) emulsions are a requirement for developing effective antioxidant solutions. Existing models do, however, not include explicit equations that account for composition and structural features of O/W emulsions. To bridge this gap, a mechanistic kinetic model for lipid oxidation in emulsions is presented, describing the emulsion as a one-dimensional three phase (headspace, water, and oil) system. Variation in oil droplet sizes, overall surface area of oil/water interface, oxidation of emulsifiers, and the presence of catalytic transition metals were accounted for. For adequate predictions, the overall surface area of oil/water interface needs to be determined from the droplet size distribution obtained by dynamic and static light scattering (DLS, SLS). The kinetic model predicted well the formation of oxidation products in both mono- and polydisperse emulsions, with and without presence of catalytic transition metals.

1. Introduction

Modelling of lipid oxidation has recently gained much attention to estimate the oxidative stability of food oil-in-water (O/W) emulsions, especially since this is the format in which oils are mostly consumed (McClements, 2015). Lipid oxidation commonly progresses faster in emulsions than in vegetable oils (Bao & Pignitter, 2023; Boerkamp et al., 2022; Villeneuve et al., 2023) and is therefore a major factor for the deterioration of the sensorial quality of such oil-containing food products. O/W emulsions consist of oil droplets that are surrounded by a thin water-oil interfacial layer and dispersed in a water phase (Berton-Carabin, Ropers, & Genot, 2014) (Fig. S1). Many compositional and structural factors can influence lipid oxidation in such systems (Hennebelle et al., 2024). Known compositional factors are the degree of unsaturation of oil, the presence of pro-and anti-oxidants in the water and oil phases and the type and partitioning of adsorbed versus nonadsorbed emulsifiers. Structural factors comprise thickness and structure of the water-oil interface, droplet sizes, and transport properties of the water phase. Furthermore, conditions such as temperature and pH can modulate lipid oxidation kinetics. Thus, to model lipid oxidation in emulsions, these factors need to be accounted for. Recent efforts in modelling lipid oxidation in food emulsions, however, only partially accounted for structural features describing the water-oil interface (Bravo-Díaz et al., 2015; Merkx, Swager, Van Velzen, Van Duynhoven, & Hennebelle, 2021; Romsted & Bravo-Díaz, 2013; Schroën & Berton-Carabin, 2022).

In literature, two main types of modelling approaches have been employed to describe the formation of oxidation products in food O/W emulsions (Bravo-Díaz et al., 2015; Merkx et al., 2021; Schroën & Berton-Carabin, 2022). The first approach uses descriptive functions to model the formation of hydroperoxides and aldehydes (Merkx et al., 2021). The second approach uses underlying kinetic reactions designed to simulate the formation of hydroperoxides and conjugated dienes in O/W emulsions stabilized with different emulsifiers (Schroën & Berton-Carabin, 2022). These existing models fit well but cannot predict the formation of oxidation products when applied to different O/W emulsion samples.

Despite the fact that many experimental studies have examined droplet size dependency of lipid oxidation under different conditions, the conclusions from different sources appear contradictory and cannot

* Corresponding author. *E-mail address:* marie.hennebelle@wur.nl (M. Hennebelle).

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be explained by these existing models (Atarés, Marshall, Akhtar, & Murray, 2012; Costa, Freiría-Gándara, Losada-Barreiro, Paiva-Martins, & Bravo-Díaz, 2020; Horn, Barouh, Nielsen, Baron, & Jacobsen, 2013). This is because these existing modelling approaches did not include equations that explicitly describe transport phenomena and interactions such as the impact of pro-oxidant concentration in the water phase that will be influenced by specific emulsion structural features such as droplet sizes (Hennebelle et al., 2024). The first mechanism, i.e., transport phenomena, relates to the amount of e.g., O2 absorbed into the water-oil interface that depends, in principle, on the ratio between the total surface area of the emulsion and oil phase volume, in other words, on the droplet sizes (Cengiz, Hennebelle, Berton-Carabin, & Schroën, 2023). This dependence is also true for other water-soluble molecules such as e.g., excess emulsifiers or prooxidants (Gambardella, Ganzeveld, Winkelman, & Heeres, 2005). It has been observed that emulsions with a larger surface area, i.e., smaller droplet size, show faster lipid oxidation (Horn et al., 2013; Ten Klooster et al., 2023; Ten Klooster et al., 2024). It is clear that the total surface area of the emulsion can have a large effect on lipid oxidation. The second mechanism concerns the reactions of dissolved O2 with unadsorbed emulsifiers (Donbrow, Azaz, & Pillersdorf, 1978) and water-soluble molecules (Gambardella et al., 2005) in the water phase. These reactions can directly influence the amount of O₂ available for lipid oxidation, and indirectly the amount of oxidation products reacting with pro-and anti-oxidants.

The aim of this study is to develop a model that can address the aspects described above. To do this, we extend our previous mechanistic kinetic model that simulates the formation of oxidation products in bulk oils (Nguyen et al., 2023) to include the aspects described above in a one-dimensional three phase (headspace, water, and oil) system. As in the bulk oil model, explicit equations describing the effects of fatty acid composition, iron ions, tocopherols, and O2 mass transfer mechanisms are used. The extended model also incorporates equations to describe the number of water-soluble molecules absorbed into the water-oil interface according to the droplet size, and the consumption of O₂ by water-soluble molecules (i.e., Tween 20 used as an emulsifier and Fe-EDTA used as oxidation initiator). The ability of the model to describe the effect of overall interfacial area on the lipid oxidation rate is evaluated by simulating lipid oxidation in both mono- and polydisperse O/W model emulsions stabilized by Tween 20. The accuracy of the model simulations is then evaluated by comparing them with experimental data

2. Material and methods

2.1. Datasets

Two datasets with different droplet sizes with and without Fe-EDTA were used. The datasets were obtained from recent studies on lipid oxidation in O/W emulsions in which hydroperoxides, aldehydes, epoxides, and headspace O_2 were measured (Ten Klooster et al., 2024; Ten Klooster et al., 2023).

The first dataset was acquired by incubating 387.5 μ L of 10% rapeseed O/W emulsion (pH 7.0) stabilized with 2 wt% Tween 20 and 12 mM of Fe-EDTA, which were initially added in the water phase (Ten Klooster et al., 2024). The ratio 1:1 between iron ions and EDTA was based on experimental observations that this ratio changes the reactivity of Fe-EDTA complex as an oxidation catalyst (Berton, Ropers, Viau, & Genot, 2011; Berton-Carabin et al., 2014; Ten Klooster et al., 2024). These samples were incubated in closed 1.75 mL polypropylene tubes with an initial O₂ partial pressure of 21% in the headspace. Shelf-life experiments were conducted in the dark without agitation at 25 °C for 14 days. Monodisperse and polydisperse O/W emulsions were prepared by a lab-scale microfluidic emulsification (Fluidic, Connect PRO Chip Holder with 4515 Inserts, Micronit Microfluidics, Enschede, The Netherlands). The O₂ partial pressure in the headspace was monitored with a MOCON OpTech-O₂ oxygen sensor (Ametek Mocon, Brooklyn Park, MN, USA).

The second dataset was acquired by incubating 10 mL of 10% rapeseed O/W emulsion (pH 7.0) stabilized with 0.5 wt% Tween 20 without Fe-EDTA complex (Ten Klooster et al., 2023). The samples were incubated in 20 mL headspace vials with an initial O_2 partial pressure of 21% in the headspace, in the dark, without agitation at 25 °C for 20 days. The incubation time took longer than the incubation time in the first dataset due to the absence of oxidation catalyst (Fe-EDTA). The polydisperse O/W emulsions were prepared by a lab-scale colloid mill emulsification (IKA Magic Lab, Staufen, Germany) and a high-pressure homogenizer (M-110Y Microfluidizer, Microfluidics, Massachusetts, USA).

These datasets were split into training and test datasets, as summarized in Table S1. In our previous study (Nguyen et al., 2023), many different training datasets were used to estimate kinetic constants of reactions with C18:1n-9, C18:2n-6, and C18:3n-3, at 20 and 40 °C. These data were used to infer the kinetic constants at 25 °C used in this study. A single training dataset (total O/W surface area of $\sim 26 \text{ m}^2$, monodisperse containing Fe-EDTA, Table S2) was used to estimate the remaining parameters. These are kinetic constants for O₂ reactions with Tween20 and Fe-EDTA in the water phase, partition coefficient of Fe-EDTA between the water and oil phases, and kinetic constants for Fe-EDTA reactions in the oil phase. The test dataset consisted of monodisperse (total O/W surface areas of 5.5 and 2.8 m², containing Fe-EDTA), and polydisperse emulsions (total O/W surface areas of 2.8 and 0.9 m² containing Fe-EDTA and of 1.19 \times 10³ and 2.32 \times 10³ m² without Fe-EDTA, Table S2). This test dataset was used to evaluate the correctness of the model in simulating the changes in kinetic of lipid oxidation associated with changes in droplet sizes.

2.2. Analyses

Hydroperoxides and aldehydes were quantified in duplicate by ¹H NMR with relative standard deviations (RSD) of ~5.9% (Merkx, Hong, Ermacora, & Van Duynhoven, 2018), and epoxides were quantified in duplicate by 1 H- 13 C HSQC NMR (RSD \leq 11.6%) (Boerkamp et al., 2022). The limit of detection (LOD) for lipid hydroperoxides and aldehydes was 0.01 mmol/kg oil (Merkx et al., 2018) and for epoxides was 0.19 mmol/ kg oil (Boerkamp et al., 2022). In the training dataset and test datasets 1-4 (Table S1), the oil droplet sizes of the emulsions (Figs. S4 and S5) were measured by light microscopy (Ten Klooster et al., 2024). In test dataset 5 (Table S1), the overall droplet size distribution of the whole emulsion sample was derived from the three following steps. First, the droplet size distribution (>100 nm) of the whole emulsion (without centrifugation) was measured by static light scattering (SLS) (Malvern Mastersizer 3000, Malvern Instruments Ltd., Malvern, Worcestershire, UK) (Ten Klooster et al., 2023). Second, the smallest oil droplets (10 to 360 nm, Fig. S6) separated from the larger oil droplets by centrifuging the whole emulsion were then measured by dynamic light scattering (DLS) (Zetasizer, Nano ZS, Malvern Instruments Ltd., Malvern, Worcestershire, UK) (Ten Klooster et al., 2023). Finally, the overall droplet size distribution for the whole emulsion sample was obtained by combining the SLS and DLS results, as described previously (Yang et al., 2023) (Fig. S7). In this combination, the relative intensities from the DLS measurements were adjusted based on the actual oil content of the emulsion sample of very small droplets. The relative intensities from the SLS measurements were adjusted using the assumption that its oil content was one minus the oil content of the emulsion sample of very small droplets.

2.3. Model assumptions

The following assumptions were made to extend the model for lipid oxidation in bulk oil (Nguyen et al., 2023) to O/W emulsions: (1) the O/W emulsion system is considered as a three phase headspace-water-oil system (Fig. 1); (2) the timescale of diffusion of O_2 and reactants was



Fig. 1. Schematic representation of the three phase system used to model O/W emulsions. A, a schematic drawing of an actual O/W emulsion in which oil droplets are dispersed in a water phase and topped by a headspace volume. B, Representation of the three phase headspace-water-oil system used in the model, as simplification of the real emulsion shown in A.

assumed to be very fast compared to the sampling timescale. Thus, all reactants are considered to be uniformly distributed in the phase in which they are dissolved (i.e., O2 in all three phases, radicals and oxidation products in the oil phase, and iron ions and Fe-EDTA in the water and oil phases); (3) To describe lipid oxidation, all molecules present in bulk phase as well as at the water-oil interface are considered to react with the same kinetic constants as in bulk oil model (Nguyen et al., 2023); (4) The kinetic constants of Fe^{3+} and Fe^{3+} -EDTA complex were assumed to be 100 times lower than the kinetic constants of Fe²⁺ and $\mathrm{Fe}^{2+}\text{-}\mathrm{EDTA}$ complex, respectively. This assumption was done based on literature (Choe & Min, 2006), as well as to reduce possible redundancy in the model parameters. The iron ions will have different reactivity in the complex than in the free state. Thus, the kinetic constants of reactions with free iron ions (kpro1 and kpro2, Table 1) were considered to differ from the kinetic constants of reactions with the Fe-EDTA complex (kpro3 and kpro4, Table 1). The Fe-EDTA complex refers to the total concentration of Fe²⁺-EDTA and Fe³⁺-EDTA.

2.4. Lipid oxidation reactions in O/W emulsions

The reactions used in this model are listed in Table 1. The model describing the oxidation in bulk oil takes into account primary (R1-R3) and secondary oxidation (R4-R10), inhibition (R11-R13), catalysis (R14-R15), and termination reactions (R18-R20) (Nguyen et al., 2023). The model was extended by including the reactions catalyzed by the oxidation initiator in the oil phase (R16 and R17), as well as the oxidation reactions of the emulsifier and catalyzer in the water phase (R21 and R22) (Donbrow et al., 1978; Gambardella, Winkelman, & Heeres, 2006, Gambardella et al., 2005).

2.5. Model construction

To describe the lipid oxidation in the emulsion in modelling, O/W emulsions (Fig. 1A) are considered as a one dimensional three phase headspace-water-oil system that is separated by two boundary layers (Fig. 1B). The oil phase in this case includes both the droplet interior and the interfacial region. The next sections explain the O_2 mass transfer processes across the three phases depending on droplet sizes.

2.5.1. O_2 mass transfer in the headspace phase

For the headspace, two O_2 mass transfer processes were considered, one through the cap (O_2 permeability and/or leakage), and the other between the headspace and water phases (**Fig. S1**). The concentration of O_2 in the headspace phase over time is described by the following rate equation (in m⁻³.mol.s⁻¹):

$$\frac{d\left[O_{2,HS}\right]}{dt} = \frac{1}{V_{HS}} \left(\varphi_{O_2}^{Pe} + \varphi_{O_2}^{HS,W}\right) \tag{1}$$

where $\varphi_{O_2}^{p_e}$ and $\varphi_{O_2}^{HS,W}$ (in mol.s⁻¹) are the kinetic rates of the changes in O₂ concentration through the cap and between the headspace and water phases, respectively; V_{HS} (in m³) designates the volume of the headspace phase.

First, the O₂ permeability/leakage $\varphi_{O_2}^{Pe}$ (in mol.s⁻¹) reflects the change in O₂ concentration between the headspace and the external atmosphere over time through the cap (Boerkamp et al., 2022; Nguyen et al., 2023), expressed as:

$$\varphi_{O_2}^{P_e} = k_{Pe} \left(p_{O_2,\infty} - p_{O_2,HS} \right) \tag{2}$$

where k_{Pe} (in mol.s⁻¹.Pa⁻¹) is the O₂ permeability/leakage coefficient, $p_{O_2,\infty}$ and $p_{O_2,HS}$ (in Pa) are the O₂ partial pressure in the external atmosphere and the headspace, respectively.

Second, the O₂ solubilization $\varphi_{O2}^{HS,W}$ (in mol.s⁻¹) reflects the exchange of O₂ between the headspace and the water phase over time, expressed as:

$$\varphi_{O_2}^{HS,W} = k_{O_2} \frac{A_{HS,W,I}}{RT} \left(p_{O_2,HS,W} - p_{O_2,HS} \right)$$
(3)

where $A_{HS,W,I}$ denotes the headspace-water surface area (m²), R (8.314 J. mol⁻¹.K⁻¹) is the ideal gas constant, *T* (in K) is the storage temperature, and k_{O_2} is the O₂ solubility coefficient in water (e.g., 4.38×10^{-8} in mol. m⁻³.Pa⁻¹ at 20 °C) (Simpson, Almonacid, Acevedo, & Cortés, 2004).

2.5.2. O_2 mass transfer in the water phase

The O_2 concentration (in m⁻³.mol.s⁻¹) in the water phase over time was described by Eq.(4). It consisted of O_2 dissolved in the water and oil phases (**Fig. S1**) and of O_2 reactions with reactants (R21 and R22 in Table 1).

$$\frac{d[O_{2,W}]}{dt} = -\frac{1}{V_W} \left(\varphi_{O_2}^{HS,W} + \varphi_{O_2}^{W,O} \right) - \frac{d[O_{2,Tween20}]}{dt} - \frac{d[O_{2,FeEDTA,W}]}{dt}$$
(4)

in which $\varphi_{O_2}^{W,O}(\text{in mol.s}^{-1})$ is the change in O₂ concentration over time between the water and oil phases, V_W (in m³) designates the volume of water phase; the kinetic rates (in m⁻³.mol.s⁻¹) of O₂ consumed by reactions with Tween 20 and Fe-EDTA complex in the water phase (R21 and R22 in Table 1) were expressed using the following second order reactions, respectively:

$$\frac{d\left[O_{2,Tween20}\right]}{dt} = k_{Tween20}n_{Tween20}[Tween20]\left[O_{2,W}\right]$$
(5)

Table 1

Overview of reactions in the presence of Fe-EDTA complex (an oxidation catalyst) and Tween 20 (an emulsifier) in the water phase and lipid oxidation reactions in the oil phase as explained in model assumption (3). The terms 'k' represent kinetic constants of the reactions. Lipid substrates LH represent specific types of unsaturated fatty acids, i.e., C18:1n-9, C18:2n-6, and C18:3n-3.

I. Lipid oxidation reactions		
1. Primary lipid oxidation reactions		
Initiation	$LH \xrightarrow{k_i} L^{\bullet} + H^{\bullet}$	(R1)
Formation of hydroperoxides	$L^{\bullet} + O_{2,O} \xrightarrow{k_{p1}} LOO^{\bullet}$	(R2)
	$\text{LOO}^{\bullet} + \text{LH} \xrightarrow{k_{p2}} \text{LOOH} + \text{L}^{\bullet}$	(R3)
2. Secondary lipid oxidation reactions		
Degradation of hydroperoxides	$\text{LOOH} \xrightarrow{k_d} \text{LO}^{\bullet} + \text{OH}^{\bullet}$	(R4)
	$OH^{\bullet} + LH \xrightarrow{k_{p3}} L^{\bullet} + H_2O$	(R5)
Formation of aldehydes	$LO^{\bullet} + LH \xrightarrow{k_a} AD + L^{\bullet}$	(R6)
Formation of epoxides	$\mathrm{LO}^{\bullet} \stackrel{\mathrm{k}_{\mathrm{cl}}}{\to} \mathrm{EP}^{\bullet}$	(R7)
	$EP^{\bullet} + LH \xrightarrow{k_{\circ 2}} EP + L^{\bullet}$	(R8) ^a
	$EP^{\bullet} + O_2 \xrightarrow{k_{c3}} EPOO^{\bullet}$	(R9)
	$EPOO^{\bullet} + LH \xrightarrow{k_{c4}} EPOOH + L^{\bullet}$	(R10)
3. Inhibition, catalysis and termination		
Antioxidant	$\text{LOO}^{\bullet} + \text{AH} \xrightarrow{\text{k}_{\text{AHII}}} \text{LOOH} + \text{A}^{\bullet}$	(R11)
	$LO^{\bullet} + AH \xrightarrow{k_{AH2}} LOH + A^{\bullet}$	(R12)
	$L^{\bullet} + AH \xrightarrow{k_{AH3}} LH + A^{\bullet}$	(R13)
Redox cycle (pro-oxidation)	$\text{LOOH} + \text{Fe}^{3+} \xrightarrow{\text{kprol}} \text{LOO}^{\bullet} + \text{H}^{+} + \text{Fe}^{2+}$	(R14)
	$\text{LOOH} + \text{Fe}^{2+} \xrightarrow{k_{\text{pro2}}} \text{LO}^{\bullet} + \text{OH}^{-} + \text{Fe}^{3+}$	(R15)
	$\text{LOOH} + \text{Fe}^{3+}\text{-EDTA}_{O} \xrightarrow{k_{\text{PO}}} \text{LOO}^{\bullet} + \text{H}^{+} + \text{Fe}^{2+}\text{-EDTA}_{O}$	(R16)
	$\text{LOOH} + \text{Fe}^{2+}\text{-EDTA}_{O} \xrightarrow{k_{\text{prod}}} \text{LO}^{\bullet} + \text{OH}^{-} + \text{Fe}^{3+}\text{-EDTA}_{O}$	(R17)
Termination	$L^{\bullet} + L^{\bullet} \xrightarrow{k_{il}} LL$ (non-radical products)	(R18)
	$L^{\bullet} + LOO^{\bullet} \xrightarrow{k_{22}} LOOL$ (non-radical products)	(R19)
	$\text{LOO}^{\bullet} + \text{LOO}^{\bullet} \xrightarrow{k_{3}} \text{LOOL} \text{ (non-radical products)} + O_{2}$	(R20)
Reactions in the water phase		
Autooxidation	$Tween20 + n_{Tween20}O_{2,W} \stackrel{k_{Tween20}}{\rightarrow} oxidation \ products \ of \ Tween20$	(R21) ^b
	$4Fe^{2+}$ -EDTA _W + O _{2 W} + 2H ₂ O $\stackrel{k_{FeEDTA,W}}{\rightarrow}$ Fe ³⁺ -EDTA _W + 4OH ⁻	(R22) ^c

Subscripts W and O for Fe-EDTA and O2 indicate the compounds in the water and oil phases, respectively.

^aReaction (R8) is expected to be much slower than R9, but was included in the model as experimental data showed the significant formation of mono-epoxides (EP) (Boerkamp et al., 2022; Nguyen et al., 2023). ^{b,c} Reactions of O_2 with Tween 20 and Fe-EDTA complex in the water phase are reported in literature (Donbrow et al., 1978; Gambardella et al., 2006, Gambardella et al., 2005), and were therefore included in the model. Reaction R21 follows an independent second-order kinetic law, in which terms 'n' represent the apparent stoichiometric coefficients (unitless), and terms 'k' represent the kinetic constant (mol⁻¹.s⁻¹.m³).

$$\frac{d[O_{2,FeEDTA,W}]}{dt} = k_{FeEDTA} n_{FeEDTA} [FeEDTA_W] [O_{2,W}]$$
(6)

where $n_{Tween20}$ and n_{FeEDTA} represent the apparent stoichiometric coefficients (unitless) and $k_{Tween20}$ and k_{FeEDTA} represent the kinetic coefficients (m³.s⁻¹.mol⁻¹) of Tween 20 and Fe-EDTA complex, respectively.

2.5.3. Mechanisms in the oil phase

2.5.3.1. Total surface area of droplets calculated from the oil droplet size distribution. The oil droplet size distribution in the emulsions using the DLS and SLS was expressed as a distribution of the volume fraction per diameter, i.e., a data tabular of *N* specific diameters (d_i in m where i = 1, N) and their respective frequencies (in %). We then converted the frequency into fraction $fraq_i$ (i.e., frequency/100 in unitless) that describes how often a specific volume (V_i) has been identified over a specific range of d_i :

$$fraq_i(V_i) = \frac{n_i \times V_i}{V_i^{total}}$$
⁽⁷⁾

where V_O^{total} (in m³) designates the volume of total oil droplets dispersed in the water phase and n_i (unitless) is the number of droplets of diameter d_i .

The total interfacial area of spherical oil droplets (A_{W,O} in m²) was

calculated from the oil droplet size distribution (Eqs. S1 to S7):

$$A_{W,O} = 6 \times V_O^{total} \times \sum_{i=1,N} \frac{fraq_i}{d_i}$$
(8)

The surface-volume mean diameter (D[3,2] in m) corresponds to:

$$D[3,2] = \frac{\sum_i n_i d_i^3}{\sum_i n_i d_i^2},$$
(9)

2.5.3.2. O_2 mass transfer in the oil phase. The change in O_2 concentration over time (in mol. s⁻¹.m⁻³) between the water and oil phases was expressed:

$$\frac{d[O_{2,O}]}{dt} = -\frac{1}{V_O} \left(\varphi_{O_2}^{W,O} + \varphi_{O_2}^O \right)$$
(10)

where $\varphi_{O_2}^0$ (in mol.s⁻¹) are the kinetic rate of the change in O₂ concentration at the oil phase that involves reactions R2 and R9 in Table 1; V_O (in m³) designates the volume of oil phase.

2.5.3.3. The distribution of reactants between the water and oil phase. The change in concentration over time $(m^{-3}.mol.s^{-1})$ of Fe-EDTA complex between the water and oil phases depends on $A_{W,O}/D[3,2]$ ratio (i.e., surface area of water-oil interface oil volume) in a similar expression to gas flux:

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$$\frac{d[\text{Fe-EDTA}_O]}{dt} = -k_{MC} \frac{A_{W,O}}{D[32]} ([\text{Fe-EDTA}_W] - K_{PC}[\text{Fe-EDTA}_O])$$
(11)

where $[\text{Fe-EDTA}_O]$ and $[\text{Fe-EDTA}_W]$ designate the concentrations (in mol. m⁻³) of Fe-EDTA complex in the oil phase and in the water phase, respectively; k_{MC} (in m.s⁻¹) is the mass transfer coefficient in the oil.

The relative percentage of number moles (%) of Fe-EDTA in the water phase (%Fe-EDTA_W(t)) and in the oil phase (% Fe-EDTA_O(t)) over time t, were calculated:

$$\% \text{Fe-EDTA}_{W}(t) = \frac{\#\text{moles of Fe-EDTA}_{W}(t)}{\#\text{moles of Fe-EDTA}_{W}(t0)} \times 100\%$$
(12)

$$\% \text{Fe-EDTA}_{O}(t) = \frac{\#\text{moles of Fe-EDTA}(t)}{\#\text{moles of Fe-EDTA}_{W}(t0)} \times 100\%$$
(13)

where #moles of Fe-EDTA_W and #moles of Fe-EDTA_O are the total number moles (mol) of Fe²⁺-EDTA and Fe³⁺-EDTA in the water phase and the oil phase, respectively, at time t or initial time t0.

The kinetic rate of Fe-EDTA concentration (Eq. (11)) was derived from the partition coefficient K_{PC} (unitless) that is defined as the ratio of [Fe-EDTA_O] and [Fe-EDTA_W] at dynamic equilibrium (Tehrany & Desobry, 2004):

$$K_{PC} = \frac{[Fe-EDTA_W]}{[Fe-EDTA_O]}$$
(14)

2.5.4. Kinetic rates of lipid oxidation

The kinetic rates (in m^{-3} .mol.s⁻¹) of the three main oxidation products (i.e., LOOHs, ADs, and EPs) were the sum of the kinetic rates of the relevant underlying reactions in Table 1:

$$\frac{d[\mathbf{LOOH}]}{dt} = \mathbf{r}_3 + \mathbf{r}_{11} + \mathbf{r}_4 + \mathbf{r}_{14} + \mathbf{r}_{15}$$
(15)

$$\frac{\mathrm{d}[\mathbf{A}\mathbf{D}]}{\mathrm{d}t} = \mathbf{r}_6 \tag{16}$$

$$\frac{d[\mathbf{EPs}]}{dt} = \mathbf{r}_{7,8} + \mathbf{r}_{7,9,10}$$
(17)

where [LOOH] and [AD] embody the concentrations of LOOH and AD, respectively, while [EPs] embodies the sum of epoxide (R8) and hydroperoxyl epoxide (R10) concentrations.

The LOOH, AD, and EP concentrations were expressed as vectors for each fatty acid individually (Nguyen et al., 2023). In this study, we focused only on oleic (C18:1n-9), linoleic (C18:2n-6), and alphalinolenic (C18:3n-3) fatty acids, as they are the most abundant unsaturated fatty acids in vegetable oils. The kinetic rate vectors (**r**) were obtained by describing the chemical reactions (in Table 1) as first order reactions (for R1, R4, and R7) and second order reactions for the remaining reactions (Eqs. **S7** to **S14**).

2.5.5. Estimation of the model parameters

The kinetic constants of reactions R1-R15 and R18-R20, in Table 1 at 20 and 40 °C were previously estimated in bulk vegetable oils (Nguyen et al., 2023), and were used to calculate the kinetic constants at 25 °C using Arrhenius equations (**Fig. S3**). Thus, only 8 additional parameters needed to be estimated to complete the extended model: k_{Pe} (Eq. 2), $k_{Tween20}$ and $n_{Tween20}$, k_{FeEDTA} (Eqs. 5 and 6), k_{pro3} and k_{pro4} (R16 and R17, in Table 1), k_{MC} , and K_{PC} (Eqs. 11 and 14).

These 8 additional parameters were estimated using a global multiresponse optimization method, by fitting the training datasets (**Table S1**) of O₂ headspace, hydroperoxide (LOOHs), aldehyde (ADs), and epoxide (EPs) profiles simultaneously, using MATLAB 2021b software (Mathworks, Natick, MA, USA). The starting values of the 8 parameters required for the optimization were obtained from the literature. Kinetic constants from previous studies were estimated using a simplified scheme of lipid oxidation reactions and models that differ from the present model, so kinetic constants in our model are not expected to be the same. As reported in literature, kinetic constants k_a (R6, Table 1) and $k_{EP} = k_{e1} \times k_{e2}$ (R7 and R8, Table 1) vary from 3.3×10^{-5} to 0.03 and from 0.032 to 3.3, all in mol^{-1} . $m^3.s^{-1}$, respectively (St. Angelo, 1992). However, these kinetic constants can be used to set the initial values of our model parameters included in the optimization procedure (Eqs. (18)–(20)). For every set of starting values, the 'lsqnonlin' algorithm was used to determine their estimated values by simultaneously minimizing the sum of the squared residuals between the experimental (X_{exp}) and numerical (X_{num}) datasets. The datasets (\widetilde{X}) were normalized (following Eq. 17) before calculating the sum of squared errors (Eq. 18), as each squared residual was in different value scales. Since each set of starting values returned different estimated values, the optimal estimated values were selected based on the least estimate of errors (Eq. 18).

$$\widetilde{X}_{i} = \frac{X_{i} - \min(X_{exp})}{\max(X_{exp}) - \min(X_{exp})}$$
(18)

where subscript *i* denotes either a numerical or experimental curves, and *exp* represents experimental kinetic curves.

$$\left\|\widetilde{X}_{\exp} - \widetilde{X}_{num}\right\|_{2}^{2} = \sum_{i=1}^{n_{f}} \left(\widetilde{X}(t_{i})_{\exp} - \widetilde{X}(t_{i})_{num}\right)^{2}$$
(19)

where t, i, and n_t indicate storage time, index of time points, and the total number of time points, respectively. After fitting the numerical and experimental datasets, the confidence of the estimated values was evaluated using Monte Carlo simulations with 200 iterations to calculate the standard deviations:

$$X_{\text{noise},exp} = X_{\text{exp}} \pm \sigma r \tag{20}$$

where $X_{\text{noise},exp}$, and X_{exp} are the noised and original experimental data, respectively. σ is the experimental standard deviation of the test dataset and r is an arbitrary normal distribution obtained from two uniform distributions in which values vary between 0 and 1 using Box-Muller algorithm (Box & Muller, 1958).

2.5.6. Evaluation of the prediction model

After the final model (Eqs. 1 to 16) parameters were estimated, the model was evaluated by comparing the predicted values for the formation of LOOHs, aldehydes, and epoxides in the oil phase to the experimental values of the test dataset (as summarized in **Table S2**).

The precision of the model when predicting the formation of oxidation products was evaluated using the normalized root mean square errors (NRMSEs) between the model outcomes and the test datasets (**Table S2**) (Nguyen et al., 2023). In particular, three tests were conducted, beginning with monodisperse samples containing Fe-EDTA (test dataset 1 and 2), followed by polydisperse samples without Fe-EDTA (test dataset 5 and 6), and finally polydisperse samples containing Fe-EDTA (test dataset 3 and 4). When oxidation catalysts (Fe-EDTA) were not added to the samples, their kinetic rates in the model were set to 0 (in Eqs. (6) and (11)).

For all three tests above, the kinetic constants used were those estimated from the training dataset. To obtain model predictions for different systems, only the initial droplet sizes were changed in the model, which in turn resulted in changes in total interfacial area $(A_{W,O})$ and average droplet diameters (D[3,2]). This further leads to changes in the Fe-EDTA partition between the water phase and oil phase using Eqs. (11) and (14). All these effects then resulted in differences in the kinetics of lipid oxidation.

3. Results and discussion

3.1. Estimation of the model parameters

The kinetic constants **k** (in R1-R15 and R18-R20, Table 1) at 25 °C were calculated from the kinetic constants previously determined at 20 and 40 °C (Nguyen et al., 2023) using Arrhenius equations, as illustrated in **Fig. S3**. The experimental data (**Fig. S2**) showed that the % of O₂ partial pressure in headspace tends to 0 after 14 days, corresponding to the time at which the maximum concentration of oxidation products of ~295 mmol/kg oil was reached. This is consistent with the initial O₂ concentration in the headspace of the closed vials of 295 mmol/kg oil. In other words, no O₂ permeability/ leakage was observed, so k_{Pe} (i.e., O₂ permeability/leakage coefficient described in Section 2.5.5) was set to 0. The 7 remaining parameters (i.e., $k_{Tween20}$, $n_{Tween20}$, k_{FEEDTA} , k_{pro3} , k_{pro4} , k_{pC} , and K_{FEEDTA}) were estimated by fitting the model (Eqs. 1–16) to the training datasets, for all experimental input data simultaneously, as illustrated in **Fig. S2**.

3.2. Oxidation prediction on monodisperse emulsions containing Fe-EDTA with different oil droplet sizes

The correctness of model predictions was tested for monodisperse emulsions containing Fe-EDTA. In the shelf-life tests, Fe-EDTA was added to accelerate lipid oxidation in the emulsion samples, so to describe this catalyst effect, we included the distribution of Fe-EDTA between phases in the model. The monodisperse samples in the test datasets 1 and 2 (**Table S1**) only differed in the total surface area; monodisperse emulsions with small (D[3,2] = 4.65 μ m) and medium (D [3,2] = 9.1 μ m) oil droplet sizes were included, corresponding to a total O/W surface areas of 5.5 and 2.8 in m², respectively, each per 387.5 μ L of an emulsion sample (**Table S2**).

The value of surface area were then used in the model following Eqs. (7) and (8), as the only variable. The surface area affects the O_2 dissolution (that is linked to the amount of O_2 in the headspace according to Eqs. (3), (4), and (10), **Fig. S1**) and the concentration of Fe-EDTA (Eq.

Table 2

Val	ues o	of th	e mod	el pa	rameters	; at	25	°C	estimated	from	the	final	mod	el.
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Model parameters*	# double bonds					
$(m^3.mol^{-1}.s^{-1})$	1	2	3			
k _i	1.1×10^{-29}	1.1×10^{-29}	1.1×10^{-29}			
k _{p1}	100	35	110			
k _{p2}	$1.2 imes10^{-5}$	$3.5 imes10^{-4}$	$8 imes 10^{-5}$			
\mathbf{k}_{d}	$3.3 imes10^{-13}$	$9 imes 10^{-14}$	$9 imes 10^{-14}$			
ka	0.002	0.002	0.002			
k _{EP} **	0.012	0.018	0.005			
k _{EPOOH} **	10^{-13}	10^{-13}	10^{-13}			
k _{pro2}	$5 imes 10^{-13}$	$8.3 imes10^{-13}$	$3.3 imes10^{-12}$			
k _{pro4}	$6.5 imes10^{-11}$	$1.95 imes 10^{-9}$	$2.6 imes10^{-9}$			
n _{Tween20}	25	25	25			
$\mathbf{k}_{\text{FeEDTA,W}}$	$5.5 imes 10^{-7}$	$5.5 imes10^{-7}$	$5.5 imes10^{-7}$			
$\mathbf{k}_{\text{Tween20}}$	$5 imes 10^{-8}$	$5 imes 10^{-8}$	$5 imes 10^{-8}$			
\mathbf{k}_{MC}	9.025×10^{-12}	9.025×10^{-12}	9.025×10^{-12}			
K _{PC}	0.3	0.3	0.3			

*In the oil phase, the initial concentrations of total iron ions = 0.02 ppm (as we used the datasets of the same rapeseed oils dispersed in the water phase) (Hoppenreijs, Berton-Carabin, Dubbelboer, & Hennebelle, 2021). Since to-copherols = 0 ppm (as oils were stripped (Berton et al., 2011)), we set the kinetic constants of reactions with antioxidants, i.e., k_{AH1} , k_{AH2} , and k_{AH3} , to be 0. Initial concentrations of oxidation products were collected from experimental data at initial time. The standard deviations of the estimated kinetic constants (Eq. (20)) were < 1%, indicating that the optimization is robust enough for the estimation of the constants.

** $\mathbf{k}_{\text{EP}} = \mathbf{k}_{e1}\mathbf{k}_{e2}$ (Eq. S10) and $\mathbf{k}_{\text{EPOOH}} = \mathbf{k}_{e1}\mathbf{k}_{e3}\mathbf{k}_{e4}$ (Eq. S11).

(11)) in the oil phase. Apart from D[3,2] and total O/W surface area (calculated from the oil droplet size distributions, Fig. S4), all other model parameters had the same value as for the training dataset (Table 2). The model without any fitting was then used to calculate the % of O2 headspace and the formation of LOOHs, aldehydes, and epoxides. The calculated or predicted values were in good agreement with the test dataset with acceptable NRMSEs (< 0.1). According to the experimental data (open circles, Fig. 2), the monodisperse samples of smaller oil droplets have more O₂ dissolution (Fig. 2A1), which allows faster formation of LOOHs, aldehydes, and epoxides (Fig. 2A2-A4). As a result, the plateau of LOOH formation of smaller oil droplets is reached earlier for smaller droplets. In addition, the droplet size affects the total concentration of $Fe-EDTA_O$ in the oil phase. This is the result of the larger surface area, while maintaining the same partition coefficient. The model was initially set with 100% Fe-EDTA in the water phase; then, according to Eq. (11), some Fe-EDTA partitioned into the oil phase until reaching an equilibrium (Fig. 2B1-B2). As there are currently no experimental data about this distribution, it would be valuable to have this data in the future.

The model outcomes indicate that the equations incorporated in the final model for lipid oxidation in monodisperse O/W emulsions adequately described the interplay between oil droplet sizes, O_2 mass transfer processes, and the distribution of water-soluble molecules between phases.

3.3. The importance of droplet size distribution for modelling polydisperse emulsions without Fe-EDTA

In the previous section, it was shown that lipid oxidation data in the monodisperse emulsion system were well-described by the onedimensional model of the three phase headspace-water-oil system. In this section, the validity of this model to describe lipid oxidation in polydisperse emulsions was tested. This is done as a step towards ultimate application of the model to industrial or commercial emulsions, which are typically polydisperse.

The total surface areas of oil droplets of the whole emulsions and emulsions after centrifugation (to remove the largest droplets >300 nm) were 2.32×10^3 m² and 1.19×10^3 m², respectively, per 10 mL of an emulsion sample. The total O/W surface areas of oil droplets in polydisperse emulsions were calculated following Eqs. (7) and (8) from the oil droplet size distribution (**Fig. S7**).

As the initial concentrations of iron ions and epoxides were not known in test datasets 5 and 6, these initial concentrations had to be estimated by fitting the model to the experimental data (squares and circles, Fig. 3). In the model fitting, the remaining parameters were kept at the same values than in Table 2 since the shelf-life conditions were similar to the training datasets. The model fitting (solid and dashed lines, Fig. 3) yielded $C_{Fe2+} = 2.21 \times 10^{-5}$ and $C_{EPs} = 0$ for the whole emulsions (test dataset 5) and $C_{Fe2+} = 7.18 \times 10^{-5}$ and $C_{EPs} = 0$ for emulsions after centrifugation (test dataset 6), all in mmol/kg oil.

We first examined whether the method used to calculate the surface area affects the model outcomes, i.e., the formation of LOOHs and aldehydes. For the whole emulsions, the total surface area was calculated from the oil droplet size distribution (**Fig. S7**) and using the formula $6 \times V_0^{total}/D[3,2]$, separately. This yielded two very different values, i.e., 2.32×10^3 m² based on the oil droplet size distribution and 245.45 m² based on D[3,2]. The model using the total O/W surface area of 245.45 m² calculated from $6 \times V_0^{total}/D[3,2]$ in which $D[3,2] = 0.05 \,\mu$ m (Eq. (9)) failed to describe the test data (dashed lines, **Fig. S8**). This illustrates the sensitivity of the model outcomes to the method used to evaluate the total O/W surface area.

We then addressed the question of which method is the most accurate to estimate the total O/W surface. When using the total O/W surface area of $1.13 \times 10^3 \text{ m}^2$ obtained with SLS only (i.e., droplet size >300 nm), the model failed to describe the test data (gray lines, **Fig. S8**).



Fig. 2. A. Model predictions without fitting (lines) versus experimental profiles (open circles, test datasets 1 and 2 in **Table S2**) of the monodisperse emulsions with small (D[3,2] = $5.02 \,\mu$ m, blue) and medium (D[3,2] = $9.14 \,\mu$ m, dark orange). Predictions are based on parameters listed in Table 2; no adjustments were made to fit the data. (A1) % O₂ partial pressure in the headspace, (A2) total LOOHs, (A3) total aldehydes, and (A4) total epoxides. B. The relative change in the Fe-EDTA concentration between the water and oil phases. (B1) % of Fe-EDTA_w concentration remaining in the water phase (Eq. (12)) and (B2) % of absorbed Fe-EDTA_o concentration over time in the oil phase (Eq. (13)). The Fe-EDTA concentration refers to the total concentration of Fe²⁺-EDTA and Fe³⁺-EDTA. Note that the scale of the y axis between the sub-figures is different. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)



Fig. 3. The concentrations of LOOHs (A1) and aldehydes (A2) over time of the whole emulsions (black squares and lines) and emulsions after centrifugation (blue circles and lines) without Fe-EDTA. Model fitting (solid lines) versus experimental data (squares and circles) of LOOHs (A1) and aldehydes (A2) using the total O/W surface area calculated based on the oil droplet size distribution (>10 nm, black solid lines; < 300 nm, blue solid lines) using both SLS and DLS. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Indeed, in these whole emulsions, very small droplets (< 300 nm) had a volume fraction of ~5.1% in the droplet size distribution, but contributed to ~51.3% of the total surface area (**Fig. S7**) (Ten Klooster et al., 2023). When taking them into consideration in the total O/W surface area (i.e., $2.32 \times 10^3 \text{ m}^2$ based on both DLS,< 300 nm and SLS, >300 nm), the model provided a more accurate prediction of the test data (blue lines, **Fig. S8**). The discrepancies in model outcomes (i.e., the blue and gray lines, **Fig. S8**) thus highlight the significant contribution of very small oil droplets to the total O/W surface area, and therefore to changes in O₂ mass transfer process (Eq. (10)) and the distribution of reactants (Eq. (11)) between the water and oil phases. It is therefore essential to experimentally determine the complete droplet size distribution including very small droplets for the correctness of the model outcomes when applied to polydisperse emulsions.

3.4. Oxidation prediction on polydisperse emulsions containing Fe-EDTA with different droplet sizes

In previous tests, the correctness of the model predictions was evaluated for the monodisperse emulsions containing Fe-EDTA with different droplet sizes and the polydisperse emulsions without Fe-EDTA with very small oil droplets.

In this section, the model was thus applied to describe lipid oxidation in polydisperse emulsions containing Fe-EDTA with different droplet sizes (test datasets 3 and 4, **Table S1**). In the test datasets, the polydisperse samples of smaller droplets have more O_2 dissolution in the oil phase (open circles, Fig. 4A1) resulting in faster formation of LOOHs, aldehydes, and epoxides (open circles, Fig. 4A2-A4). The polydisperse emulsions used had large (D[3,2] = 26.1 µm) and medium (D[3,2] =



Fig. 4. Model predictions using the model parameters in Table 1 without any fitting (lines) versus experimental profiles (open circles, test datasets 3 and 4 in **Table S1**) of the polydisperse emulsions with medium (D[3,2] = 9.14μ m, dark orange), and large (D[3,2] = 26.01μ m, dark green) oil droplet sizes. (A1) % O₂ in the headspace, (A2) total LOOHs, (A3) total aldehydes, and (A4) total epoxides. The relative change in the Fe-EDTA concentration between the water and oil phases: % of Fe-EDTA_W and % of Fe-EDTA_O over time in the water phase (B1) and in the oil phase (B2), respectively. The Fe-EDTA concentration refers to the total concentration of Fe²⁺EDTA and Fe³⁺EDTA. Note that the scale of the y axis between the sub-figures is different. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

9.14 μm) oil droplet sizes, corresponding to the total O/W surface area of 0.972 and 2.8 m², respectively, each per 387.5 μL of an emulsion sample (**Table S2**). The changes between polydisperse samples in these data were only in the total O/W surface area, resulting in changes in O₂ dissolution (Eq. (10)) and the total concentration of Fe-EDTA (Eq. (11)) in the oil phase.

Apart from D[3,2] and total O/W surface area (**Figs. S5**), all other model parameters had the same value as for the training dataset (**Table 2**). Without any fitting, the model predictions for the % of O₂ in the headspace and the formation of LOOHs, aldehydes, and epoxides were in good agreement with the test dataset with acceptable NRMSEs (< 0.1) (Fig. 4). As indicated in Eq. (11), smaller droplets that have a higher ratio between $A_{W,O}$ and D[3,2] have more O₂ dissolution in the oil phase (as illustrated in solid lines, Fig. 4A1), leading to faster formation of oxidation products (solid lines in Fig. 4A2-A4). In addition, as observed in the first test, the droplet size affects the total concentration of Fe-EDTA in the oil phase (Fig. 4B1-B2), while maintaining the same partition coefficient K_{PC} estimated in Table 2.

The model outcomes indicates that the equations incorporated in the final model for lipid oxidation in polydisperse O/W emulsions containing Fe-EDTA adequately described the interplay between droplet sizes, the O_2 mass transfer processes, and the distribution of water-soluble molecules between phases.

4. Conclusion

Our previously established mechanistic kinetic model to describe lipid oxidation in bulk oils was extended to describe lipid oxidation in O/W emulsions. Our three phase headspace-water-oil model comprises explicit equations that simulate the interrelation between the O_2 mass transfer processes, O_2 consumed by water soluble molecules, distribution of catalytic transition metals, and the ratio between the total O/W surface area and oil droplet sizes. Variations in oil droplet sizes can indeed affect the O_2 mass transfer and in turn the kinetic rates of reactions. The kinetic model predicted well the formation of oxidation products (i.e., lipid hydroperoxides, aldehydes, and epoxides) in both mono- and polydisperse emulsions and accounted for variation in oil droplet size distributions, oxidation of emulsifiers, and presence of catalytic transition metals. The model outcomes also highlighted the importance of using the total O/W surface area calculated from experimental oil droplet size distribution. Of course, the model shows that the fundamental approach seems valid. If the model is to be applied to real products, the effects of distribution and activities of other reactions need to be included. The extended model is a step towards prediction of effects of composition, structure, and shelf-life conditions on lipid oxidation in complex real life food emulsions.

CRediT authorship contribution statement

Khoa A. Nguyen: Writing – original draft, Validation, Methodology, Investigation, Formal analysis, Conceptualization. Vincent J.P. Boerkamp: Writing – review & editing, Investigation, Formal analysis, Conceptualization. John P.M. van Duynhoven: Writing – review & editing, Supervision, Funding acquisition, Conceptualization. Arend Dubbelboer: Writing – review & editing, Supervision, Conceptualization. Marie Hennebelle: Writing – review & editing, Supervision, Conceptualization. Peter A. Wierenga: Writing – review & editing, Supervision, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Arend Dubbelboer and John P.M. Van Duynhoven are employed by companies that manufacture and market oil based food products.

Data availability

Data will be made available on request.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.foodchem.2024.139404.

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